IMPACT OF SCHEDULING DRUGS UNDER THE 1971 CONVENTION ON PSYCHOTROPIC SUBSTANCES — A FOLLOW-UP STUDY*

UNITED NATIONS RESEARCH AND TRAINING CENTRE
IN DRUG DEPENDENCE
NATIONAL DRUG RESEARCH CENTRE
UNIVERSITY OF SCIENCE MALAYSIA
MINDEN, PENANG
MALAYSIA.

* A study funded by the United Nations Fund for Drug Abuse Control

IMPACT OF SCHEDULING DRUGS UNDER THE 1971 CONVENTION ON PSYCHOTROPIC SUBSTANCES — A FOLLOW-UP STUDY*

edited by:
DR. V. NAVARATNAM
and
JEANETTE JAYA CHOOI GAIK

UNITED NATIONS RESEARCH AND TRAINING CENTRE
IN DRUG DEPENDENCE
NATIONAL DRUG RESEARCH CENTRE
UNIVERSITY OF SCIENCE MALAYSIA
MINDEN, PENANG
MALAYSIA.

* A study funded by the United Nations Fund for Drug Abuse Control

Original Print 1984

ISBN. 967-9979-01-6

Printed in Pulau Pinang by Sinaran Bros. Sdn. Bhd.
Published by the National Drug Research Centre,
Universiti Sains Malaysia, Pulau Pinang.

CONTENTS

ACKNOWLEDGEMENT

This study would have not been initiated, developed and completed without the kind assistance of several individuals and organizations, of whom only some have been mentioned here:-

(i) The United Nations Fund for Drug Abuse Control for financially supporting this study;

(ii) The Government of Malaysia, particularly the Vice-Chancellor, the Deputy Vice-Chancellors and staff of the University of Science, Penang, Malaysia, for providing facilities and technical services;

(iii) The Malaysian Foreign Ministry for facilitating the work of this study;

(iv) The Director and Staff, United Nations Division on Narcotic Drugs, Vienna, Austria.

(v) The World Health Organization, particularly the Director Dr. Inayat Khan and the Staff of the Division of Mental Health, Geneva;

(vi) The participating countries, particularly the individual national agencies who freely provided information and completed the survey questionnaires;

(vii) The numerous fellow scientists who assisted in the development and improvement of the questionnaires and in viewing the report we owe a major gratitude;

(viii) The International Scientific Community, including the pharmaceutical industry who readily provided existing data reports and articles which facilitated a comprehensive review.

LIST OF TABLES IN TEXT

LIST OF TABLES IN ANNEX

PREFACE

It might be worthy to recall that the international community:

Being concerned with the health and welfare of mankind,

Nothing with concern the public health and social problems resulting from the abuse of certain psychotropic substances,

Determined to prevent and combat the abuse of such substances and the illicit traffic to which they give rise,

Considering that vigorous measures are necessary to restrict the use fo such substances to legitimate purposes,

Recognising that the use of psychotropic substances for medical and scientific purposes is indispensible and that their availability for such purposes should not be unduly restricted,

Believing that effective measures against abuse of such substances require co-ordinated and universal action,

Acknowledging the competence of the United Nations in the field of control of psychotropic substances and desirous that the international organs concerned should be within the framework of the Organization,

Recognizing that an international convention is necessary to achieve these purposes,

Agreed to the enactment of the 1971 Convention on Psychotropic Substances to which countries could become parties.

The 1971 Convention was envisaged to be a special international control instrument in relation to developing a unified control action over the psychotropic substances, whereby the *major aims* being to control the production, marketting (sale on prescription only), exportation and importation of these substances listed in its schedules.

Article 2 Sections 4 and 5 outline the criteria that need to be satisfied *before* a substance or group of substances can be listed for international control. It further identifies the international organs responsible for the conduct of the relevent evaluative functions.

During the debate at the Seventh Special Session of the United Nations Commission on Narcotic Drugs, February 1982, as well as that at the Thirtieth Regular Session, February 1983, concern was expressed about the lack of comprehensive and rigorous information to facilitate the decision making process of the Commission.

In 1982, the Commission on Narcotic Drugs adopted a resolution 2(S-VII) on procedures to be followed by the Commission on Narcotic Drugs in matters on scheduling of narcotic drugs and psychotropic substances. To further clarify its requirements, at the 1983 meeting of the Commission on Narcotic Drugs, the Commission adopted Resolution 4(XXX) on Procedures to be followed by the Commission on Narcotic Drugs in matters of scheduling the benzodiazepines.

Subsequent to the 1982 Meeting of the UNCND, interested member states Scientist and Staff of the Secretariat of the Commission, discussed possible avenues of addressing the request of the Commission. It was noted that the National Drug Research Centre, University of Science Malaysia, a designated United Nations/World Health Organisation Research and Training Centre was already executing a UNFDAC supported study on psychotropic drug assessment. It was considered that the Centre, an appropriate vehicle, should expand its scope of activities and develop an appropriate procedure for the generation and analysis of relevent information, necessary for the Commission, and prepare and independent report on its findings in collaboration with appropriate United Nation and other specialised agencies.

In response to this request the 1982/83 Impact Study was initiated and data gathering procedures developed. At the 30th Regular Session of the UNCND held in February 1983, the report of the project was presented entitled "IMPACT OF SCHEDULING DRUGS UNDER THE 1971 CONVENTION ON PSYCHOTROPIC SUBSTANCES — THE BENZODIAZEPINES REAPPRAISED".

Since several members of the UNCND expressed the opinion that the report had facilitated their work, to continue to facilitate the work of the UNCND, and to respond to Resolution 4(XXX) a Second Impact Follow-Up Study was conducted.

The financial support for the conduct of this study which was provided by the United Nations Fund for Drug Abuse Control is gratefully acknowledged.

This study reviewed all the benzodiazepines as well as pentazocine which was being placed before the UNCND for consideration for international control.

In accordance with the requirements outlined in the 1971 Convention, the report presented here has assembled and analysed data from various sources including data provided by participating countries in the Impact Follow-Up Study; provided information on:

i. The pharmacology, toxicity and therapeutic use;

ii. Overuse, abuse potential and the extent of abuse and their consequences, social and public problems, as well as illicit drug traffic. Existing data, as well as new data are critically examined in relation to the general problem of drug abuse to ascertain the real extent to which it causes social and public health problem;

iii. The extent to which national legislation can effectively address the problems of benzodiazepine and pentazocine abuse and the effectiveness and usefulness of international control in addressing these same problems;

iv. The economic, social, legal and administrative aspects as well as the impact of controlling the benzodiazepines and pentazocine internationally was assessed.

In persuance of Article 2, Section 5 of the 1971 Convention on Psychotropic Substances, we have the honour to present this report entitled "A Follow-Up Study" for the information and use of the United Nations Commission on Narcotic Drugs.

1. EXECUTIVE SUMMARY

It will be recalled that at the 1982 Seventh Special Session the Commission on Narcotic Drugs adopted a Resolution 2 (S-VII) on Procedures to be followed by the Commission in matters of scheduling narcotic drugs and psychotropic substances. As part of that resolution, the Commission requested member states for "information on the economic, social, legal and administrative factors related to the abuse of substances being considered for possible scheduling and to supply as completed data as possible on any illicit trafficking in the substances in question".

In response to the above resolution an Impact Study was carried out with the objectives of developing and applying a data gathering methodology so as to obtain and assess relevant information on substances being considered for control which the Commission might usefully consider. This study was reported at the 30th Regular Session of UNCND held in Vienna in February 1983 entitled "Impact of Scheduling Drugs Under the 1971 Convention on Psychotropic Substances — The Benzodiazepines Reappraised".

During the debate on this subject several members indicated the usefulness of such a study. At the 30th Regular Session of UNCND the Commission adopted Resolution 4(XXX) of February 16th 1983 entitled "Procedure to be followed by the CND in matters of scheduling of the benzodiazepines."

In support of the above mentioned resolution, and to facilitate the work of the CND; incorporating the comments received from members of the Commission, a follow-up study on the Impact of Scheduling Drugs under the 1971 Convention of Psychotropic Substances was conducted. This study was conducted by the National Drug Research Centre, as a designated United Nations/World Health Organisation Research and Training Centre for Drug Dependence; and was financially supported by the United Nations Fund for Drug Abuse Control. This study is referred to as the 1983 Impact Follow-up Study.

In accordance with the 1971 Convention on Psychotropic Substance this study and this report should be considered by the United Nations Commission on Narcotic Drug as other "appropriate source" and it should be considered as complementary and supplementary to the reports of the United Nations Division on Narcotic Drugs, the World Health Organisation as well as other national and international agencies. This study reviewed thirty-nine substances which constituted the group of benzodiazepines which were proposed by the W.H.O. for review and Pentazocine which was the only one of the narcotic mixed agonist-antagonist group of substances which was recommended by the W.H.O. Advisory Group for control. The report which is being presented to the Commission encompasses the findings of the 1983 study as well as summaries of the original Impact Study 1982.

The various findings are reported and presented in five sections namely:-

A. Benzodiazepines
B. Pentazocine
C. General Issues
D. Potential Impact of Scheduling
E. Possible directions for action

A. BENZODIAZEPINES

i. Pharmacology

The benzodiazepines, with the exception of *tibenzonium, propizepine, pyrenzepine and ethifoxine,* as a class all exert the same qualitative actions and posses a similar mechanism action, even though there are some quantitative differences in their pharmacodynamic activity. With the exceptions mentioned above, *they all cause central nervous system depression.* Recent studies have conclusively demonstrated that benzodiazepine withdrawal syndromes can be precipitated by newly developed benzodiazepine-specific antagonists. Experimental data is available for chlorodiazepoxide, diazepam, flurazepam, halazepam, lorazepam and triazolam.

ii. Pharmacokinetics and lipo-sulubility

Work at receptor sides would indicate that concentration at the receptor, rather than in the systemic circulation, is more decisive for the time course of pharmaco dynamic action (effect kinetics). Factors like half-life of blood concentrations and lipo-solubility which have been used in arguments to differentiate different benzodiazepines, have not, to-date, been supported by clinical evidence.

iii. **Therapeutic Use**

The benzodiazepines are used as a therapeutic agent in a wide spectrum of clinical situations. These include life-saving situations such as tetanus in adults and newborns in status epilepticus, and some in drug intoxications.

iv. **Dependence Liability**

It is clear, from the available evidence, that all those benzodiazepine substances being recommended for control produce a state of dependence.

v. **Extent of Use**

BALTER et. al. (1983) reported on a study of benzodiazepine use in the USA and 10 European countries. This study reported that it was clear that there was a decreasing trend in the prevalence rate of past year use from 1971 to 1981. It was also being reported that in relation to the pattern of use, short term use (3 months and less) was more frequent than long term use. These results have been verified for the USA, where D.M. SMITH (1982) reported that overall use of benzodiazepines has dropped in excess of 30% between 1973 and 1980, and past year use prevalence also decreased. Several researchers including PETERSSON and LADER have deep concerns about long duration of use, a phenomena which is reported to be increasing specifically in the UK in contrary to other Western European countries.

vi. **Illicit Traffic and Abuse**

Consistent with the previous study, existing data on illicit traffic, availability and extent of abuse was reviewed. In relation to illicit traffic, 40 countries reported the existence of such activities in relation to the benzodiazepines. In nearly all instances, illicit traffic also indicated illegal availability within their national boundaries. Reports of illicit traffic/availability existed for 20 benzodiazepines substances. These were bromazepam, chlordiazepaxide, clobazam, clonazepam, clorazepate, cloxazolam, diazepam, estazolam, flunitrazepam, flurazepam, ketazolam, lorazepam, medazepam, nimetazepam, nitrazepam, oxazepam, oxazolam, prazepam, temazepam and triazolam. An attempt was made to ascertain the quantities of the various benzodiazepines seized in illicit traffic. From the total data base it was found that twenty-five (25) countries could provide information on amounts seized. Since there was no uniformity in the quantum of reporting (i.e. dosage units, ampoules tablets etc.) one was unable to conduct a correlative analysis. However if one computes, rather crudely, the number of seizures reported by national authorities by substance type, the pattern emerging supports the view that the more widely a substance is marketted and available, the greater is the likelihood and quantities that are intercepted in illicit traffic.

A total of twenty-six (26) countries reported the existence of the problem of benzodiazepine abuse. From the information provided it was noted that twenty-two (22) out of the 33 being recommended for control had reports of being abused. Difficulties were experienced in relation to interpreting the data in relation to the frequency and severity of abuse. In respect to the individual benzodiazepine no differentiation could be made. However it was noted that there were more abuse reports for the more widely marketted, older generation benzodiazepines. This trend noted, would support the generalisation that the more widespread the use, the greater the likelihood of abuse and in these circumstances more likely is an iatrogenic abuse.

vii. **Public Health and Social Issues**

Eleven countries indicated that they were aware of fatalities with benzodiazepines. Of these 11, only 2 were in a position to give adequate information. Lorazepam, diazepam and oxazepam were more frequently associated with fatalities, whilst bromazepam, chlordiazepoxide, clorazepate, flurazepam, ketazolam, nitrazepam and temazepam have also been reported but less frequently.

HARVEY (1983) has reaffirmed that benzodiazepines were relatively safe substances and were very infrequently detected as a sole or predominant substance in overdose deaths but were more frequent as subsidiary substances. It is therefore important to distinguish those fatalities that occur solely due to these drugs from those that occur due to multiple/combination drugs, one of which could have been a benzodiazepine.

Another area of concern has been the possible impairment of driving and of the potentiation of the central nervous system depressants (e.g. barbiturates, alcohol etc.) which would lead to adverse social effects.

Benzodiazepines have not been shown to incite or induce criminal behaviour on their own.

Whilst there is good data on the abuse and dependence of benzodiazepines the assessment of public health consequences and social problems is not conclusive. Inspite of the lacunae in information, it has to be acknowledged that overuse and abuse of benzodiazepines can induce a degree of individual dysfunctionality which could have social consequences. What really is debatable is the extent and degree to which these effects manifest.

B. OPIOID — AGONISTS-ANTOGONISTS-PENTAZOCINE

i. **Pharmacology**

Pentazocine, as well as buprenophine, butorphenol, cyclazocine and nalbuphine demonstrate both analgesic and narcotic antagonist properties in animals and humans. Whilst there appears to be some quantitative differences in regards to these pharmacological actions, qualitatively they are quite similar.

Pentazocine obviously has strong nalorphine-like agonist-effects as well as possess substantial analgesic properties. Human studies have demonstrated that pentazocine resembles morphine at low doses, but shows nalorphine-like activity at higher doses. Therapeutic analgesic doses of pentazocine produces a morphine-like euphoria, without sedative or psychomimetic effects. However larger doses were nalorphine-like, with dysphoria sedation and psychomimetic effects.

From available pharmacological data it is clear that pentazocine, buprenorphine, butorphenol cyclazocine and nalbuphine are capable of inducing Central Nervous System stimulation and deperession which could result in disturbances in motor function, changes in mood and in some circumstances hallucinations.

ii. **Therapeutic Use**

The primary therapeutic use for these substances is as a pain suppressant. Pentazocine has been demonstrated to be a potent analgesic agent with the ability to suppress chronic pain.

iii. **Dependence Liability**

All the five opioid agonist-antagonists, except buprenorphine produce physical dependence when administered repeatedly. Equally all five substances will precipitate withdrawal symptoms in morphine dependent rodents and dogs but not in morphine dependent rhesus monkeys. Self administration studies have demonstrated that the opioid agonist-antagonists except cyclazocine are able to sustain drug taking behaviour, however they are clearly less reinforcing than heroin, codeine and dextropropoxyphene.

Hence it can be stated that *all the opioid agonist-antagonists with the possible exception of cyclazocine, can produce a state of dependence.*

iv **Illicit Traffic and Abuse**

Nineteen (19) countries reported the existence of illicit traffic with pentazocine. Of these nineteen, seventeen (17) also indicated that seizures had been made of pentazocine. Again difficulties were encountered in attempting to quantify these seizures. The general conclusion that could be reached was that the quantities seized varied from insignificant amounts to somewhat large seizures in the USA. Further, while tha existence of traffic was a worldwide occurrence, the overall quantities detected outside the USA were relatively small.

In relation to actual abuse, sixteen (16) countries reported that they were aware of the abuse of pentazocine in their respective countries. Of these countries, apart form the USA, only seven (7) other countries were able to provide hard data on pentazocine abusers. For 1981 and 1982, it was reported that 767 persons have been detected for pentazocine abuse outside tha United States.

v. **Public Health and Social Issues**

Consumption data for pentazocine was found to be severely lacking. Data from USA showed that therapeutic use was at the highest in 1973 with 6 million prescriptions, but the level dropped to 3.5 million for 1980. Generally the available data would indicate an overall decrease in consumption levels.

It has been shown that Central Nervous System disturbances occur with pentazocine. However psychotomimetic side effects are definitely dose related. The extent of occurrences with perceptual disturbances was below 10%. It should be pointed out the problems of perceptual disturbances were not limited to pentazocine, but also occur with other analgesics.

C. GENERAL ISSUES

i. In the 1982 study serious concerns were expressed regarding the implementation of the 1971 Convention on Psychotropic Substances. Issues such as the lack of clarity of scheduling criteria and terminology as well as its inability to tackle problems of drug overuse, imitations and counterfeits all of which contributed to the abuse problem were raised.

In the 1983 study similar concerns were reiterated and exemplified. Grave doubts were expressed to the effectiveness of Schedules III and IV of the 1971 Convention. The need for a rationalisation of the International Drug Control System was argued for by some implementing authorities. Some experts raised tha question regarding the original purpose of the 1971 Convention and its real value in assisting developing nations. Some experts were of the view that Scheduling a substance under Schedule III or IV of the 1971 Convention was in effective and did not really assist in addressing the "real" problem.

The need to distinguish an abuse problem which could better be handled through national measures rather than internatinal control was an important factor reported by some countries. The lack of real international cooperation, particularly for substances unser Schedule III and IV of the 1971 Convention was expressed.

The continuing theme appears to be one which calls for an independent assessment of the philosophy, rationale for drug control and effectiveress of implementation at international and national levels.

D. POTENTIAL IMPACT OF SCHEDULING

i. Benzodiazepines

It was reported that, with the exception of three countries, benzodiazepines were available only on medical prescription. Some countries pointed out that they had imposed additional or more stringent control measures on those benzodiazepines or benzodiazepine preparations that were reportedly being abused. Some of these countries described the negative aspects of their differential "ad hoc" additional decisions. They reported that these measures, in some instances, had resulted in illegal and legal users changing to other substances, which in some cases produced more severe problems. Their experience led them to strongly advocate a group approach it the benzodiazepines are to be scheduled. All the participants reported that international control will not affect legitimate availability for medical use.

In respect to *illicit availability* there is a difference in opinion. Some countries opined that international control will have little or no impact, whilst others feel that it would have little or no impact, whilst others feel that it would have some effect. Several agree that information gathering will be facilitated. The reservation appears to stem from the belief by several countries that their current national controls are adequate and in many cases, more stringent. As such they seen no value in international control.

Possibly for the above mentioned reason, the majority of countries gave no definite answer to the question as to whether or not benzodiazepines should be scheduled. Only four countries expressed clearly the opinion that no control was necessary. On the other hand twenty-one countries indicated acceptance and even supported for a control decision. However some were not fully convinced of the value of international control.

It is clear that there is a lot of ambivalence regarding the usefulness of controlling the benzodiazepines at this point in time. The reasoning behind this attitude would seem to emerge from the frequently held opinion that these are extremely useful and widely used therapeutic substances which would best be controlled effectively through national mechanisms rather than an international control procedure.

ii. Pentazocine

In all the participating countries, pentazocine were strictly controlled through national legislation. Again in several of these countries, based on national (local) experiences additional controls have

been imposed. In all these countries, pentazocine was still available for legitimate medical use. A significant majority of the countries indicated that, in their opinion, pentazocine should be treated as a narcotic drug and controlled in a similar manner.

Four countries reported that inspite of stringent national controls, they still evidenced non-medical use of pentazocine and three indicated that they were aware of illicit availability in their respective countries.

With respect to the *impact of international control,* every respondent opined that international control will not affect legal availability. Further several pointed out that since the current levels of their national controls were very stringent international control would only facilitate law enforcement activities. Others, opined that international control would certainly have impact on illicit traffic; hence, illicit availability and this, in itself, would curb the further spread of pentazocine abuse.

In general there is greater acknowledgement and acceptance of the need to control pentazocine than the benzodiazepines. The opinion that emerges is that, for pentazocine, international control would have a facilitating effect.

E. POSSIBLE DIRECTIONS FOR ACTION

The 1971 Convention under Article 2 Sections 4 and 5 clearly lays down the information on which decision to include a substance or group of substances for international control must be based.

(i) The Benzodiazepines

All the *33* benzodiazepines being recommended for international control clearly fulfill the requirements outlined in Section 4(a) 1 and 2.

Further for 22 of these substances there was actual evidence of abuse, and for the remaining 11 substances there was clinical evidence of dependence or evidence which would support that they had the likelyhood to be abused and hence causing public health and social problems. Thus the requirement of Section 4(b) of the Convention are fulfilled.

The Commission has to review the available information to determine whether Article 2 Section 5 is fulfilled before a decision to include or exclude can be achieved. In considering this aspect the Commission may which to take note of the following:

(i) The concern expressed about the effectiveness of the 1971 Convention and in some instance the reported administrative difficulties.

(ii) The therapeutic usefulness of the benzodiazepines.

(iii) The opinion expressed by some nations that for this group of substances, national control measures were more effective than international controls.

(iv) Whether the extent and degree of the public health and social problems were globally widespread and that international control will facilitate the reduction and control of these problems.

Weighing the evidence in toto, it is clear that the Commission must give equal weightage for all the 33 benzodiazepines and irrespective of the decision, it must apply to all of them. Taking into cognisance all available elements of information from the viewpoint of science, the Commission can adopt one of the following alternatives.

(i) Schedule all the 33 benzodiazepines as recommended by the World Health Organisation since they fulfill the key requirements of the Convention.

(ii) Defer the decision to schedule the group of benzodiazepines but continue to carefully monitor the prevalence of abuse as well as associated public health and social problems on a periodic basis, (e.g. biannual)

Irrespective of the decision the Commission should establish procedures to continuously monitor the patterns and consequential effects of the abuse of the benzodiazepines as well as the impact of international control. Further, the Commission should seek ways and means of strengthening national control, particularly in developing countries, in order to ensure that requirements as outlined by the 1971 Convention can be effectively implemented by them.

(ii) Pentazocine

Pentazocine, as well as buprenorphine, butarphenol and nalbuphine clearly fulfill the requirements outlined in Section 4 a(1) and (2) of Article 2 of the 1971 Convention. Cyclazocine partially fulfils these requirements.

There is actual evidence of abuse for pentazocine; however there is good evidence to support the view that buprenorphine, butorphenol and nalbuphine have the capacity to be abused; and hence Section 4(b) of Article 2 in the 1971 Convention was fufilled.

The Commission should review the available evidence to determine whether or not Article 2 Section 5 was fulfilled before reaching a decision. However, prior to this, the Commission should examine the basis on which W.H.O. have recommended only pentazocine for international control.

In evaluating the evidence the Commission may wish to take the following into consideration:—

(i) Whilst reports of pentazocine abuse are widespread, the problem is significant in the U.S.A. There are only a scattering of reports from the rest of the world.

(ii) If pentazocine alone is controlled, than there may be a shift to the other opioid agonist-antagonists and hence a change in the abuse pattern rather than reduction.

(iii) That several countries were on the opinion, that pentazocine should be considered as a narcotic drug and if this is accepted, was the 1971 Convention the appropriate instrument for its control.

Reviewing the decision options open to the Commission, the following are worthy of consideration:

(i) Schedule pentazocine as recommended by W.H.O.; and

(ii) Defer the decision to schedule pentazocine and request W.H.O. to conduct a comprehensive and systemmatic review of all the opioid agonist-antagonists taking into account the consequences of shifting abuse patterns.

CONCLUSION

This is one of the few occasions that the United Nations Commission On Narcotic Drugs is faced with deciding whether or not to control a group of substances which are extremely similar and that have, particularly with the benzodiazepines a wide therapeutic use. From the research evaluation efforts presented in this report, it is clear that there are numerous methodological lacunae. Clearly from the experimental view point the results of animal and human studies show contradictions. This is to be expected since the changes measured, while being reliable and apparent, are not dramatic as those seen for heroin, amphetamine, dextropropoxifine etc. Further the public health and social consequences are much more masked with these substances which make it difficult to differentiate consequences of poor bad therapy from those that manifest directions from illicit use. Data on abuse also is more poorly documented and reported.

It is for these reasons that The United Nations Commission on Narcotic Drugs, should, irrespective of the decision, support the need for the conducting of carefully designed monitoring studies of these substances in a selected number of countries as well as the impact of international control on therapeutic behaviour.

2. BENZODIAZEPINES: SUMMARY AND UPDATE

a. Pharmacology, Therapeutic Use and Dependence Liability

(i) Summary of the 1982 Study

The main findings of *experimental pharmacology* reported in the Impact Study 1982 can be summarised as follows.

The benzodiazepines as a class of drugs all exert the same qualitative actions and possess a similar mechanism of action, even though there are quantitative differences in their pharmacodynamic activity. They are all central nervous system depressants. Their most characteristic and specific action is the disinhibition or the normalisation of behavioural responses suppressed previously by punishment or by absence or reward. This has been interpreted as an anxiolytic and an anti-frustration activity. This specific benzodiazepine activity is not exhibited by other groups of psychoactive drugs, with minor exceptions such as alcohol, barbiturates and a few others. However, this latter group of drugs exhibits a very narrow range of dissociation between anticonflict and unspecific "sedative" effects.

Benzodiazepines produce various effects which are categorized clinically as "sedative", but in experimental pharmacology are termed "reduced arousal". Furtermore they are potent blockers of epileptic convulsions and have a muscle relaxant effect in hypertonic (decerebrate) as well as in normotonic (normal) animals. They reduce the autonomic response to direct electrical stimulation of the hypothalamus, and autonomic reflexes by peripheral stimulation. This is the rationale for the use of benzodiazepines in various psychosomatic disorders.

The mechanism of action consists in increasing GABA-ergic inhibition of neuronal activity and is mediated by specific benzodiazepine receptors.

Pharmacokinetics can be described most appropriately by a three compartment model.

Highly specific *benzodiazepine antagonists* have been discovered recently. They antagonise specifically benzodiazepine effects mediated by the central benzodiazepine receptors, i.e. the antipunishment, anti-convulsant, muscle relaxing and the polysynaptic depressant effects of benzodiazepines.

Among the *side effects* sedation is the most prominent at higher doses. Serious intoxication and death due to the ingestion of benzodiazepines alone are extemely rare, even with the highest overdose. However death may follow an overdose of benzodiazepines, when concomitantly alcohol and/or other drugs have been ingested.

In *therapeutic use* the four main actions of this class of drugs are anxiolytic, muscle-relaxant, antiepileptic and sedative-hypnotic. The muscle relaxing effect of benzodiazepines can be life saving in tetanus of the adult as well as in tetanus of the newborn, this latter condition being seen mainly in developing countries. Another life-threatening condition, status epilepticus, can be stopped by intravenous diazepam in almost every case. Malaria and chloroquine intoxication are causes of status epilepticus seen in developing countries. The sedative-hypnotic action has not only led to wide spread acceptance of benzodiazepine preparations as sleep inducing medication but has also been taken advantage of by anaesthetists who widely use benzodiazepines as premedication and induction agents.

In the context of therapeutic use three studies were mentioned investigating *social issues* of benzodiazepine medication in the working place, in family life and a quality of life respectively.

For *physiological dependence* on benzodiazepines, it has been stressed that comparison of experimental data is made difficult by the fact that various methodologies have been used in different studies. There was no compelling evidence to demonstrate any difference in the dependence-producing effect of various benzodiazepine antagonist Ro-15-1788 to precipitate benzodiazepine withdrawal syndromes in animals was reported. In humans, physiological dependence on benzodiazepines can develop, especially with higher daily doses and with long duration of treatment.

Psychological dependence is studied experimentally by methods observing self administration in animals and man. Controversial results were reported at some length in the Impact Study 1982. As a general result it was concluded that benzodiazepines have a low to moderate reinforcing activity; it is certainly lower than that of many other sedative-hypnotics, e.g. barbiturates. Data on dependence in humans were reported in the chapter on abuse. It was concluded that the "pharmacological, pharmacokinetic and abuse data on the dependence potential of the benzodiazepines are inconsistent and often contradictory. On the basis of the current data available, it is not possible to arrive at any distinction as to the relative dependence potential of the individual benzodazepines."

(ii) **Update** — 1983 Impact Study

Research work has progressed along the lines outlined in the 1982 Impact Study. The question of existence of *different kinds of benzodiazepine receptors* has been raised.

At present 2 types of receptors have been reported, one of them being found (surprisingly) in the kidney and other tissues. For the brain some authors propose the distinction of a Type I and Type II benzodiazepine receptor. Such finding raised more questions than they could answer. HAEFELY (1983) has recently reviewed the biological basis of benzodiazepine actions. Clearly more research work is needed to clarify the role of the receptors in relation to clinical efficacy, to the time-cause of effects and to the dependence potential of benzodiazepines. The newly developed antagonist would prove to be an important tool in such research.

The search for *endogenous ligands* to the benzodiazepine receptors has been broadened, but has not yet given an unequivocal answer. The most exciting finding would be the development of a mixed agonist/antagonist; such a substance could be expected to have a more selective action than the benzodiazepines on the market so far, e.g. having an anxiolytic without the sedative-hypnotic component. However no definite evidence for the existence of such a substance has yet been published to out knowledge.

The *antagonist substances* seem to have come into wider use in the investigation of physical dependence, because withdrawal symptoms can be produced in a more dramatic manner by giving an antagonist than by just stopping the medication. The work with the newly developed benzodiazepine antagonist Ro-15-1788 to precipitate benzodiazepine withdrawal syndromes in animals have considerably expanded during the last year by different reseachers (CUMIN; LUCAS and GRIFFITH; DAIRMAN and JUHASZ; McNICHOLAS and MARTIN; HAEFELY and CUMIN). Typical withdrawal syndromes have been demonstrated so far for chlordiazepoxide, diazepam, flurazepam, halazepam lorazepam, triazolam, in different experimental animals.

In *pharmacokinetics of benzodiazepines* a new perspective seems to be emerging from the work receptor sites. Concentration at the receptor, not in the systemic circulation, is suggested to be probably more decisive for the time course of pharmacodynamic action ("effect-kinetics").

However factors like half-life of blood concentration and liposolubility have been repeatedly used, globally as sales arguments and as arguments to differentiate between dependence liability of different benzodiazepines, in spite of the fact that these assumptions were not supported by any clinical evidence. The use of such inconclusive information has prompted the Food and Drug Authority of the U.S.A. to send a letter to firms marketing benzodiazepines in that country warning them against what FDA considers a "trend toward comparative advertising by means of representations or suggestions of clinical significance derived from non-clinical studies." FDA has particularly noted misuse of pharmacokinetic data and also some misuse of "data or conclusions based upon animal pharmacology or lipid solubility studies."... "The misuse of such comparative data in promotional materials has been and is currently the reason to deem such materials as false, lacking in fair balance, or otherwise misleading" (quoted form SCRIP, reference see FDA).

Along the same line it seems questionalble that data on kinetics of blood values can be used to argue about dependence potentials. It is obvious that more research work has to be done before a clear concept can be reached on how concentrations at different levels (blood, brain, receptor site) influence the kinetics of effects and the dependence potential.

Social issues of therapeutic tranquillizer use have been examined in a recently completed study from the Michigan Institute for Social Research (R.D. CAPLAN et. al). The study addressed the issue as to whether or not public health or social problems are associated with benzodiazepines. The study involved the interviewing of 367 Valium users and 308 non-users. The findings presented at the August 1983 Annual American Psychological Association Meeting showed persons taking Valium believed that the medication was helpful, tended not to use street drugs, and tended to take less Valium than their physician recommended rather than the exact amount or more. Furthermore daily users of Valium did consume less alcohol during the periods when they used the drug. The study produced no evidence to indicate that Valium users are unaware of feelings of become unmotivated to deal with their problems as a result of using ther medication. Also, Valium users and non-users exhibited no differences in their awareness of reality and there was no evidence that Valium use led to diminished self-esteem. Most important, however, there was no evidence of recreational use of Valium.

A series of papers published since the Impact Study 1982 have dealt with different aspects of physiological and psychological dependence, but in our opinion none of them has brought a real breakthrough.

WOODS has updated and expanded his last year's review and finalised it for publication. He continued to believe that available information is not adequate to permit a fair assessment of the abuse liability of benzodiazepines, individually or as a group. The projectability of available information is problematic, since in his opinion it is scientifically unreasonable to generalize from the fragmentary information which is available on the newer compounds. Finally, a determinative assessment of the abuse liability of benzodiazepines can reasonably

be achieved only by standardizing the methods of evaluation, and the consistent application of these methods from an early stage in the development of new benzodiazepine compounds. As to physiological dependence he was unable to draw an conclusion about quantitative differences that may develop among the various individual compounds.

To the above question the conclusion reached in the Impact Study 1982 seems to be still valid: *present evidence does not allow to distinguish between individual benzodiazepines as to their abuse liability.*

2.b. Epidemiology — Substances of Overuse?

(i) **Summary of the 1982 Impact Study**

In the Impact Study 1982 the epidemiology of benzodiazepine use, especially the question whether the benzodiazepines were substances of overuse, was examined in some detail. Even when consumption figures were available,there was a gap in knowledge between these figures and consumption patterns. Taking into consideration import figures for developing countries and Australia as reported in the 1982 Impact Study, the consumption figures for some countries showed an increasing trend while others showed a decreasing trend. The essential figures for Australia for example showed a decreasing trend but such an assumption is not clear as the figures have been extrapolated from a small, particular unrepresentative usergroup i.e. the pensioner population under the Pharmaceutical Benefits Scheme. Malaysia's consumption which was falling had been attributed to an educational campaign for critical prescription practices among Malaysian prescribers. From the few epidemiological studies available (NIDA Group, BALTER, MELLINGER et. al., UHLENHUT; HESBACHER; ALLGULANDER) there was no evidence for overprescription of benzodiazepines.

MARKS' (1981) study reported that he had reviewed prescription patterns in the UK from several field investigations and found that a relatively high proportion of patients who received over a prolonged period of time repeat prescriptios for their benzodiazepine tranquillizer, obtained their prescriptions from the receptionist of their doctor without the latter seeing them again. The theme of long term use in the UK has been taken up again by BALTER et. al. (1983) and by PETURSSON and LADER (1983) and this will be reviewed the update section.

(ii) **Update — 1983 Impact Study**

The previous *epidemiological studies on use ferquency* by the BALTER group, reported in the Impact Study 1982, were followed up by BALTER et. al. through a new study. The results were presented at the VII World Congress of Psychiatry, Vienna, July 1983, and the draft manuscript was made available to us (BALTER et. al., - Personal Communication). The paper reports findings from a 1981 cross-national survey of the use of anti-anxiety/sedative medication by adults in the general population of the United States and of ten Western European countries. The results could be easily compared to those of the earlier studies by the same group, since the methodology used was similar. However the duration of the medication was studied in more depth in this new study. Further age and sex distribution have been reported in more detail. the past year prevalence of anti-anxiety/sedative drug use (extracted from BALTER's Paper - by permission) is compared here to previous data (as reported in the Impact Study 1982):

TABLE 2(b)—I:- BALTER et. al. (1983): Prevalence rate of past year use of anti-anxiety/sedative drugs (compared with Table 3 as in Impact Study 1982, pg. 16)

Country	1981 Study % age of respondents	1971 Study as quoted in IS 1982	Rank 1981	Rank 1981 excluding Switzerland for co,parison with 1971	Rank 1971	Difference between last two columns
Belgium	17.6	17	1	1	1	0
France	15.9	17	2	2	2	0
Switzerland	14.6	*	3		*	
Spain	14.2	10	4	3	10	7
USA	12.9	15	5	4	5	1
Germany	12.0	14	6	5	6	1
Denmark	11.9	15	7	6	4	2
Italy	11.5	11	8	7	9	2
Great Britain	11.2	14	9	8	7	1
Sweden	8.6	16	10	09	03	6
Netherlands	7.4	13	11	10	8	2

* Switzerland was not included in the 1971 study.

From the above comparison it is clear that there is a decreasing trend in the prevalence rate of past year use from 1971 to 1981. The rank order of the countries and the order of magnitude of prevalence rates show a similar pattern in spite of the 10 year interval between the two studies. USA is in both studies is ranked roughly in the middle. The only two countries that have changed their relative rank position remarkably, are Sweden (decrease in users) and Spain (increase in users).

A new parameter taken into consideration in the recent study (BALTER 1983) was the duration of regular daily use. The categories were:

— less than one month (short term use)
— 1-3 months (intermediate term use)
— 4-11 months
— 12 months or more (long term use)

This parameter seems more meaningful than the point prevalence of use reported in the original 1971 study.

There was a considerable variation among countries in the prevalence of long term and short term use, but regular daily use for 3 months or less was the predominant pattern in all 11 countries. At the national level the data show the simple past year prevalence rates and the durational parameters of use are relatively independent. Sweden, with a low prevalence rate of users (rank 10) has also the highest proportion of continous use for 3 months or less, and the lowest proportion of long term users. In contrast Switzerland ranks high in prevalence rates of use (rank 3) but had one of the highest proportions of use during 3 months or less. On the other hand, Great Britain e.g. was rather low on prevalence rates (rank 9) but had a rather low proportion of users for 3 months or less and a comparatively high proportion of long term users (more than one year).

There results led the authors to suggest that questions about the extent, nature and appropriateness of drug use among persons in the general population can and should be posed in a more complex and clinically relevant manner and that multi-dimensional profiles of use variables can be very helpful in this regard, as shown here by the data on duration of continous drug use.

By introducing the new parameter of duration of continous drug treatment, additional data was generated on the prescribing and use of psychoactive drugs. It was apparent that the bulk of the use was for short duration.

Only in one country (Belgium) the proportion of the long term users (more than one year) was higher than that of the short term users (less than one month). However also in Belgium the proportion of short term and intermediate term users (up to 3 months) was higher than that of the long term users. So it can be said that to a very large extent psychoactive drugs are used n the countries investigated in a conservative way. The United States' comparison to other countries was one of the main objectives of this study. It was concluded that the US emerged as a nation that is moderate in overall prevalence rates of use, strongly disposed towards shorter periods of daily use, and average with its share of long term regular users.

The trend towards shorter periods of use in the US appears also from the fact that overall use of benzodiazepines has dropped in the US in excess of 30% between 1973 and 1980 (D.M. SMITH, 1982) while past year use prevalence decreased much less dramatically.

The measure on duration of continuous psychoactive medication is of particular importance in view of the reported likelihood dependence consequent to long term benzodiazepine medication. It is generally acknowledged that problems of dependence are absent if the duration of continuous treatment is short (less than 4 months); the problems stem mainly from long term treatment (more than one year) even here the frequency of dependence is debated.

A paper by PETURSSON and LADER (1983) on "Pattern and Extent of Tranquilliser Usage", draws largely on the work of the BALTER group, but gives some additional data. An (unpublished) survey by STOLL and LADER found in South East London a prevalence rate for past year's tranquilliser use of 9% for males and 19% for females. MARKS's studies (already quoted in the 1982 Impact Study, page 18) in the UK were analysed in some detail. On the whole the authors largely confirm the BALTER findings concerning the UK. The figures reported from Scandinavian countries are interesting. The phenomenon reported by BALTER for Sweden (sharp drop in tranquilliser prescriptions) has also been observed in Iceland. This country was reported in the 1982 Impact Study to be high in its consumption of benzodiazepines up to 1976 (see figure 3b, Page 13). According to PETURSSON and LADER "the sales figures (based on defined daily dosage, DDD) for tranquillisers in Iceland dropped dramatically from 55 DDD/1000 inh./day in 1976 to about 24 DDD/1000 inh./day in 1980 (Nordiska läkemedelsnämnden, 1982). The prescription rules for benzodiazepines in Iceland were revised in 1977, and 10mg tablets of diazepam were restricted to hospital use only. Furthermore, information regarding the appropriate indications for prescribing benzodiazepines was distributed to physicians which may also explain the relative increase in the use of antidepressants in Iceland in the last few years (Nordiska läkemedelsnämnden, 1982)."

This is a good example of the efficacy of educational and regulatory measures on a national level.

PETURSSON and LADER dealt at some length with the durational aspect of treatment in the UK and discussed what they considered "less favourable developments". Their main concern was the relatively high proportion of long term users noted. This group seems to be increasing, inspite of a decrease in the overall prescription rate for benzodiazepines. It is abudantly clear from the BALTER study that this prescription pattern is a specific problem of the UK, different from most other Western European countrias investigated and from the US.

2.c. Abuse, Public Health and Social Issues

Summary of the 1982 Impact Study

Isolated benzodiazepine abuse is much less frequent than abuse of benzodiazepines within the frame of polydrug abuse. It seems to stem almost exclusively from therapy. Careful evaluation of a case before prescribing a benzodiazepine and close monitoring thereafter should be done by the physician, but regretably this is not a universal routine.

In a survey of all Swiss prescribing physicians, LADEWIG (1981) found 180 cases of pure benzodiazepine abuse cases (less than half of them being dependent) and 254 polydrug abusers. In the latter group, significantly more negative social consequences were noted than among the cases of pure benzodiazepine abusers. From the epidemiological point of view LADEWIG (1981) was unable to find a correlation between half-life of a benzodiazepine and its abuse risk.

In polydrug abuse cases involving benzodiazepines alcohol seems to play a prominent role in Western countries and narcotic drugs in the East. Worldwide narcotic analgesics and non-narcotic analgesics seem to be more often abused than benzodiazepines. Benzodiazepines are infrequently used as primary drugs of abuse.

In reviewing this field it was stressed in the Impact Study 1982 that data were scarce and insufficient and that more data would be needed. In view of this situation the Impact Study quoted from the report of the 5th WHO REVIEW FOR PSYCHOACTIVE SUBSTANCES FOR INTERNATIONAL CONTROL (November

1981) the statement "... there is in most countries a lack of adequate information about the way in which the extent to which drugs are used and misused."

It was emphasized that the BALTER (1983) data showed no excessive use of benzodiazepines; this however did not exclude abuse. Data on use is only one indicator on abuse, and rather indirect one, so long as the abusers represent only a small fraction of the total users.

The figures on *illicit traffic* of benzodiazepines collected in the Impact Study 1982 showed that of the 27 benzodiazepine substances reviewed evidence of illicit traffic was reported for 19 of these substances for the period 1979-1981. Those benzodiazepine substances not reported or infrequently reported correlated very closely with those benzodiazepines which were less widely marketed globally. The amounts seized varied widely, but again, it was apparent that the more widely the substances were marketed the greater were the quantities that were likely to be intercepted in illicit traffic. As to *abuse* only a minority of countries (16 out of 57) reported that they were experiencing a benzodiazepine abuse problem that was causing public health concern. An analysis of the reported abuse data showed that 19 benzodiazepine substances were reported to be abused.

Combining both illicit traffic information and the abuse reports evidence for illicit traffic and/or for abuse existed for 22 out of the 27 benzodiazepine substances.

Only a small minority of countries were in a position to give a "head count" of primary benzodiazepine abusers. Caution was advocated in the use and in the extrapolation of this data. From them it was not possible to draw a conclusion that benzodiazepines on their own were causing a significant social and public health problem. More precise studies, particularly epidemiological and clinical, were thought to be necessary to determine the real extent of abuse and the associated problems. One statement which reflected the situation is reported here verbatim from the previous Impact Study:

> "The data tend to indicate that benzodiazepine abuse is minor compared to the general drug abuse problem or even opiate abuse. This is partially accurate since several countries stressed that benzodiazepine abuse was a secondary problem component to the problems associated with narcotic drugs. However, it must also be appreciated that the absence of insignificant reporting of benzodiazepine abuse, in almost all countries may be bias as most nations have developed good monitoring systems for narcotic drugs specifically but not for benzodiazepines. The occurence of benzodiazepine abuse tends to be reported peripherally through the narcotic reporting systems."

Among the *public health and social issues* reviewed in the Impact Study 1982 was data on mortality from overdosage of benzodiazepines. Statistics were in agreement over the fact that fatalities due to an overdose of a benzodiazepine alone was rare. Further the DAWN data were reviewed critically; the conclusion was that with all the "caveats" that are inherent in the DAWN system, the data generated had to be interpreted with great caution. Traffic safety was judged to be a controversial issue and more research was needed in this field. Unquestionably alcohol was a more important factor in endangering traffic safety than benzodiazepines. The combination of the two was found to impair driving ability significantly. There was no evidence that benzodiazepine use led to criminal behaviour.

UPDATE - 1983 IMPACT STUDY

LADEWIG whose 1981 study was in the Impact Study 1982 has extended his survey and has analysed his data in greater detail in a second publication (LADEWIG 1983).

Practically in all of the 180 cases of pure benzodiazepine abuse found in his survey, abuse took its origin from legitimate therapeutic use of benzodiazepines. The large majority of the abusers (about 90%) continued to take the drug for medical reasons (mainly for self-medication of anxiety and/or insomnia) but in dosages considered inappropriately high or without the consent of the reporting physician. The majority of the "abusers" with a medical motivation were socially fully functional.

Only in 20 of the 180 cases (11% of the abusing persons) benzodiazepine use was for definitely non-medical reasons, e.g. to get "stoned", 2 cases; for 4 intoxication with "switch-off", 5 cases; to get euphoric, 7 cases. The validity of this last data however is questioned by the author, because 5 of the seven cases with euphoria "were reported by the same physician, a fact which is in the statistical sense hardly understandable."

There were no deaths and no criminal behaviour among the reported consequences of abuse by this author.

LADEWIG (1983) published the following table in his paper. It gives the risk factors of dependence from prescribing benzodiazepines, calculated for the five most frequently prescribed benzodiazepines in Switzerland.

TABLE 2(c)-I

Substance	Risk Factor	Expected No. of Cases of abuse per 1 Million prescriptions
Lorazepam	0.0000211	21
Flunitrazepam	0.0000169	17
Diazepam	0.0000164	16
Oxazepam	0.0000157	16
Bromazepam	0.0000156	16

The author, from the above figures has inferred that there may be anything between 16 and 21 cases of abuse per 1 million benzodiazepine prescriptions. The figures do not allow one to make any distinction between the dependence producing potential of these various benzodiazepines.

The physcian's attitude towards the abuse fo benzodiazepines was in many cases "ambivalent, resulting in a tacit acquiescence and continued prescription."

The author draws the conclusion "that for Western European societies abuse of benzodiazepines is a cause of concern neither for public health nor for society; what causes concern is the high incidence of psychosomatic disturbances with symptoms which need some kind of treatment."

The author opined that: "From the data presented it is concluded that the most appropriate measure against the abuse of benzodiazepines would be, rather than international control, education of medical professionals and the public, according to internationally accepted medical knowledge, but to national law and prescription rules." It is rather suprising that LADEWIG reached such a conclusion, especially on the limited data available to him and only form one country i.e. Switzerland.

The LADEWIG figures can be criticised as to the denominator used to calculate the risk factor of abuse. He took prescription frequency; however the better denominator would have been the number od patients exposed to benzodiazepine therapy. This number can only be obtained in special circumstances when prescription monitoring exists. Unless prescriptions are monitored by some system (as it can be done in the UK), patient numbers are practically impossible to be determined.

Another factor, highlighted by BALTER et. al., is the popularity of drugs, i.e. the degree to which different drugs are known in the public. In table 2(c)-II BALTER et. al. have analysed data on which drug was named by individuals interviewed in that survey. It is clearly demonstrated that e.g. in the US the two oldest benzodiazepines, chlordiazepoxide and diazepam, were by far the most frequently named drugs. The popularity of these drugs is probably larger than their real consumption level. This popularity factor should be taken into account as well, when interpreting other data sources e.g. DAWN, STRIDE etc. In France, clorazepate, is the leader in popularity, while in Switzerland, diazepam, is way above oxazepam and lorazepam, which are imported products. Belgium, in contrast, shows a more even distribution with lorazepam at the top. It would appear that a multifactorial assessment of abuse factors need to be considered, taking into account consumption/market share, time since introduction, prescription frequency, number of patient exposed to each benzodiazepine, popularity, price etc. However no formula can yet be offered for this multifactorial analysis; under these circumstances prescription frequency as used by LADEWIG is probably the best of the available parameters to be sed as denominator.

LADEWIG's Swiss survey on benzodiazepine abuse is complimented by another Swiss survey, the Schweiz. Drogenbericht, published by FREY and UCHTENHAGEN in Spring 1983. It is the result from the work of a committee established specially by the Swiss Government to report on the drug situation in Switzerland. In this report benzodiazepines were mentioned only marginally. However the number of hard core heroin addicts is estimated to be around 5,700 and of alcoholics in need of treatment around 160,000. These numbers speak for themselves when compared to the 180 cases of benzodiazepines abuse identified in the second LADEWIG publication. It seems relevant to examine the question of benzodiazepine abuse in the context of the national drug abuse situation.

The information obtained in the 1983 Impact Study was examined to ascertain the extent of benzodiazepine in respect to the respective national problem of drug abuse.

TABLE 2(c)-II
PERCENTAGE DISTRIBUTION OF DRUGS BY COUNTRY
(Base: Drugs Named, 1 per person)

	Belgium	Denmark	France	Germany	Britain	Italy	Netherlands	Spain	Sweden	Switzerland	U.S.A.
Bromazepam	19.5	5.0	0.3	12.3		7.1		2.8		16.1	
Camazepam						1.3	2.1				
Chlordiazepoxide		6.2	0.7	2.2	12.9	0.6	15.5	3.7	2.8	3.6	20.0
Clobazam	2.1		4.9	0.6				1.9			
Clorazepate			50.0	3.4	3.9	3.2	1.0	15.7		1.0	
Delorazepam						7.7					
Diazepam	20.3	18.6	8.4	49.2	72.3	40.0	48.5	65.7	44.9	48.4	76.0
Estazolam			0.7								
Flunitrazepam			1.4								
Lorazepam	34.3		22.0	1.1	11.0	33.5	11.3	3.7		9.4	4.0
Medazepam			0.7				1.0			1.0	
Nordazepam						0.6					
Oxazepam	23.7	70.2	9.1	31.3		4.5	19.6		52.3	20.3	
Pinazepam						0.6		4.6			
Prazepam			0.7			0.6	1.0	1.9			
Tofisopam			1.0								
Totals	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Total No. of Drugs Named	236	161	286	179	155	155	97	108	107	192	125

Source: Cross-National Study of Ante-anxiety Medication, 1981 BALTER et. al. oral presentation.

In the 1982 Impact Study data was collected on the general drug abuse situation, on illicit traffic and abuse of benzodiazepines and on the consequential social and public health problems perceived by the participating countries. This procedure was repeated and extended in the 1983 Impact Study, the rationale being to review the information needed for Article 4b of the 1971 Convention on Psychotropic Studies.

From data gathering during the 1983 Impact Study Table 2(c)-III has been constructed. It gives the list of drugs/substances the participating countries considered to be commonly abused, in order of importance.

In the majority of countries opiates, barbiturates, cannabis, amphetamines and methaqualone are the major drugs of abuse. Only half the countries even listed benzodiazepines as substances of abuse, and in nearly all the countries they ranked at or near the bottom.

In relation to the non-medical use of benzodiazepines, 11 countries reported that they had some evidence. Two countries (Hong Kong and New Zealand) did not consider benzodiazepines as a problem. Of those countries that had evidence of non-medical use, Canada, Nigeria, Norway and Senegal considered it as primarily an iatrogenic problem rather than a problem of primary abuse.

TABLE 2(c)-III
The Drugs/Substances commonly abused in order of importance according to country.

Australia
1. Alcohol
2. Tobacco
3. Cannabis
4. Barbiturates
5. Amphetamines
6. Tranquilisers

Burma
1. Opium
2. Heroin
3. Marijuana
4. Others, including psychotropic substances

Canada
1. Cannabis and Derivatives
2. Ephedrive-Phenylpropenalamine Caffeine
3. Opiate Analgesics including Pentazocine
4. Cocaine
5. Amphetamine and Congeners
6. Hallucinogens (LSD, MDA, etc)
7. Heroin
8. Benzodiazepines
9. Barbiturates
10. Methaqualone.

India
1. Methaqualone
2. amphetamines
3. Secobarbital

Malaysia
1. Heroin
2. Ganja
3. Opium
4. Morphine
5. Sedatives
6. Other stimulants

Norway
1. Cannabis resin
2. Amphetamine
3. Heroin
4. Cocaine

Philippines
1. Marijuana
2. Corex D
3. Hycodin
4. Hylorin
5. Diazepam
6. Ornacol
7. Peracon
8. Pomilar
9. Endotussin
10. Nitrazepam

New Zealand
1. Cannabis & derivatives
2. Pethidine
3. Barbiturates
4. Morphine
5. LSD
6. Opium
7. Heroin
8. Methadone
9. Solvents

Thailand
1. Opium
2. Heroin
3. Diazepam (injectables)
4. Amphetamines
5. Secobarbital
6. Barbiturate
7. Meprobamate
8. Nitrazepam

Nigeria
1. Indian hemp stimulants
2. Barbiturates/ benzodiazepines

Hong Kong
1. Heroin

Continuation: TABLE 2(c)-III

The Drugs/Substances commonly abused in order of importance according to country.

Pakistan	Senegal	Singapore
1. Hashish	1. Amorarbital	1. Heroin
2. Opium	2. Secobarbital	2. Opium
3. Heroin	3. Flunitrazepam	3. Cannabis
4. Barbiturate	4. Dermocorticoides	4. Flunitrazepam
5. Methaqualone		
6. Mandrex		
7. Morphine		

Available data from several sources, including the 1983 Impact Study was reviewed to ascertain the extent and nature of the problems of illicit drug traffic and abuse of benzodiazepines. It should be recalled that Article 4(b) of the 1971 Convention on Psychotropic Substances requires "that there is sufficient evidence that the substances is being or likely to be abused .... warranting the placing of the substance under International Control."

Consistent with the previous approach, existing data on illicit availability and extent of abuse was reviewed. Reports of governments to the United Nations Secretary-General as well as to Interpol for 1981/82/83 were used as part of the data base.

In relation to illicit traffic 40 countries reported the existence of such activities in relation to the benzodiazepines (Table 4(iii)) in the ANNEX. In nearly all instances, illicit traffic also indicated illegal availability within their national frontiers. Further reports of illicit traffic/availability existed for 20 benzodiazepine substances (Table 4(i))in the ANNEX. These were bromazepam, chlordiazepoxide, clobazam, clonazepam, clorazepate, cloxazolam, diazepam, estazolam, flunitrazepam, flurazepam, ketazolam, lorazepam, medazepam, nimetazepam, nitrazepam, oxazepam, oxazolam, prazepam, temazepam and triazolam. Among these countries that reported illicit traffic, some countries including Canada, Malaysia and United States reported that their illegal availability was attributable in part to both diversions from licit sources as well as counterfeits. Four countries (Canada, Malaysia, Hong Kong, U.S.A.) had evidence that benzodiazepines may have been used as counterfeits of other substances and vice-versa. Singapore and Philippines opined that their illegal availability was consequential to illegal importation/smuggling from external sources.

An attempt was made to ascertain the amounts of the various benzodiazepines interdicted in the illicit drug traffic. From the total data base, (i.e. including data from the 1982 and 1983 Impact Studies) it was found that twenty-five countries could provide information on amounts seized. Table 4(iia) in the ANNEX and Table 4(iib) in the ANNEX provides the required analysis. It would be noted that the manner in which the seizure data was reported varied from dosage units, ampoules, tablets and even actual weight. The most comprehensive and comparable data was provided by these countries who participated in the 1982.1983 Impact Studies. Since the quantities seized could not be analysed systemmatically, one could not reach a definative conclusion on the severity of the problem of illicit drug traffic, except to note that it is relatively widespread. Further if one computes the number of seizure reported by national authorities by substance type, the pattern emerging supports the view that the more widely a substance is marketted and available, the greater is the likelihood and quantities that are intercepted in illicit traffic.

Abuse Data

Again reviewing the total data base available to the study, it was found that 26 countries reported the existence of a benzodiazepine abuse problem (see Table 4(iii)) in the ANNEX. Further, of these countries only 15 considered that there were some, often minimal social and public health problems associated with benzodiazepine abuse.

Table 4(iv) in the ANNEX provides the analysis of reported abuse data with the various benzodiazepines. From this analysis it was noted that 22 out of the 32 benzodiazepines recorded were reported to be abused. It must be stressed here that the reports of abuse were difficult to interpret with respect to frequency and severity of abuse. For most of the substances only 1 or 2 countries reported problems of abuse. However it was obvious that the older generation, more widely marketed benzodiazepines there were more reports of abuse. The finding would support a generalisation that the more widespread the use, the greater the likelihood of abuse and in these instances most likely iatrogenic abuse.

An attempt was made in the 1983 Impact Study Follow-up to quantify the extent and severity of benzodiazepine abuse as it had been done previously. Table 4(vi) in the Annex gives this information. It was found that of the 22 countries who reported the existance of a benzodiazepine abuse problem, only eleven (11) could provide a head count. Hong Kong, Malaysia and the Philippines provided data for both 1981 and 1982. Both

Hong Kong and Malaysia showed a decrease in the number of benzodiazepine abusers being recorded. However, Philippines showed marked increase in the level of abuse. From a methological point of view, only the availability of trend data would allow one to predict whether there was an increase in the abuse of a substance or substances. In this instance, the fact that only 3 countries could give data for at least a two year period, does not allow one to make any sound judgement on the extent and chronicity of the problem. Obviously only by monitoring these group of substances would one be able to reliably generate information that would allow a sound decision to reached. This certainly is not the case for the present.

From the total data base, an analysis was undertaken to correlate the number of reported benzodiazepines abuse cases with drug type. Table 4(v) in the ANNEX gives the necessary information. Nine (9) countries were in a position to provide this data. It can be seen 18 benzodiazepines substances have been individually identified with abusers. However for the majority the numbers reported are extremely small. Only for six of these substances where the case reports exceeding one hundred. Interestingly, it was noted that the substances which had accumulated larger number of reports were in fact those products that were pioneers in the field and also, not suprisingly, having the greatest market penetration. The only exception to this would be triazolam which was a relativley recent entry into the market, however it is heavily utilised – 14 million patient months since introduction and marketed in over 57 countries. Hence it would appear that in reality, one is unable to differentiate any one of the 34 benzodiazepines being recommended for control by the World Health Organisation, to an extent that one could state that a particular substance was less likely to be abuse then its counterparts. If anything the data, limited as it is, seems to support a view that abuse accurrence seems to correlate more with the depth and breadth of market penetration.

The problem of determining the prevalence of benzodiazepine abuse were numerous, the assessment of the social and public health ramification was more complex as it will be seen next.

Public Health and Social Issues

Mortality data is one indicator that can be used to assess consequences of abuse. Eleven countries indicated that they were aware of fatalities with benzodiazepine. Of these eleven, only two (Australia and the U.S.A.) were in a position to give adequate information. Lorazepam, diazepam and oxazepam were more frequently reported with fatalities, whilst bromazepam, chlordiazepoxide, chlorazepate, flurazepam, ketazolam, nitrazepam and temazepam have been associated with fatalities. The question that should be raised here is whether the absence of data from other countries was consequent to their not having an adequate organization to collect, retrieve and trasmit such information *or* due the real absence of fatalities due to benzodiazepine abuse. Since benzodiazepines are generaly considered safe drugs, it is important that when one examines fatalities due to benzodiazepines it is essential we distinguish those fatalities that occur solely due to these drugs; from those that occur due to the ingestion of multiple/combination drugs one of which could have been a benzodiazepine.

The data provided by Australia was generated through a carefully conducted study, as such much realiability can be placed on it. In contrast the data from the United States were more difficult to interpret. In general the data shows that there is a greater chance for fatalities to be reported with these benzodiazepine mortalities has been presented in the 1982 Impact Study.

A recent study by HARVEY (1983) is worthy of review. In this study, he surveyed all overdoses and other drug related deaths in Central London (population 2.7 million) from 1977 to 1982. In this area about 31,000 death occur yearly of which 10,000 are reported to the coroner and about 1,800 are subject of a coroner's inquest. He reported that while the overall overdose death rate remained rather stable form 1977-1982, the percentage of addicts among the overdose deaths increased from 15% in 1977 to 33% in 1982. Barbiturate overdoses (more than one third in 1977) decreased considerably (15% in 1982). The Table 2(c)-IV has been compiled from figures reported by HARVEY.

This study supported the view that benzodiazepines were rather safe substances and were very infrequently detected as a sole or predominant substance in overdose deaths. However they have been relatively frequently reported as a subsidiary associated with overdose death.

In relation to perceived or actual social and public health problems, countries reported that they were concerned about these problems which were, in their opinion, consequential to benzodiazepine abuse. Further 27 countries, whilst acknowledging possible social and public health consequences due to the abuse of benzodiazepines, said that they did not consider these problems as significant within their territories.

However only four countries provided explanations for their concern. Australia reported that while benzodiazepines are not frequently used as primary durgs of abuse they were, however, abused in conjunction with other drugs and alcohol. They stated that "abuse of benzodiazepines in a secondary context is sufficient to warrant concern." Two principal areas of concern expressed were "possible impairment of driving and potentiation of central nervous system depressants (principally barbiturates and alcohol) taken in therapeutic amounts (an increasing number of fatalities are occuring due the accidential overdosage)."

TABLE 2(c)-IV **Substances found at post mortem or directly implicated in the death of an addict in Central London**

	1978-1979		1981-1982	
	As sole or predominant substance	**As subsidiary substance**	**As sole or predominant substance**	**As subsidiary substance**
Morphine	58	10	90	5
Barbiturate	68	13	42	6
Methadone	15	17	19	10
.....				
Benzodiazepines	2	37	3	38
.....				
Solvents	4	2	13	1
Alcohol	-	54	-	60
.....				
Total	193	133	167	120

Bahrain opined that because the benzodiazepines could cause public health and social problems they should be strictly controlled. No specific public health or social problems were cited.

Sweden reported that according to an investigation conducted in 1977, that the persons who had gotten a prescription of hypnotic-sedatives, 2.9 per mille during a five year period developed a pattern which seemed to indicate abuse. There were no figures available on the prevalence of abuse of different hypno-sedatives in the general population in Sweden. The rates of mortality and morbidity among benzodiazepines abusers were reported to be high and capacity of work had decreased for a considerable proportion of the patients. "Available data indicate that abuse of hypnotic-sedatives now mainly concerns the benzodiazepine group and that this is a considerable problem in the psychiatric field."

The United States reported on the extensive use of 12 benzodiazepines on the US market and on problems connected therewith. According to their report benzodiazepines "are rarely the drug of choice of drug abusers ... the main use pattern among poly-drug abusers and opiate addicts are probably associated with self-medication efforts to counteract drug withdrawal effects. Also benzodiazepines are often a drug of deception in that they are reformulated to a dosage form made to resemble methaqualone." Further they noted that "the basic risk associated with the class of benzodiazepines is, in part, a function of use patterns." It is the opinion of the Food and Drug Administration Advisory Committee that there are no data to support any one compound as having a greater or lesser risk associated with it. When used at therapeutic dose levels, these drugs are very safe. However, the risks rise significantly when a second CNS depressent and/or alcohol is introduced.

Argentina provided excellent toxicological information on the association of substance abuse with public health and social problems (GARCIA FERNANDEZ 1983). He had studied toxicological cases referred to the analytical Toxicological Center since 1973. Since that date 11,020 cases have been analysed. It was reported that 284 cases were identified with depressant drugs. Of this group 74 cases (26.1%) were related to benzodiazepines. However in the context of the total case load this represented only 0.67%. In relation to attempted suicides it was reported that benzodiazepine associated suicides increased from 5 cases in 1975 to 12 cases in 1982. The total number of cases detected where benzodiazepines alone or in combination with other drugs was 56.

Other South American countries were not in a position to provide similar information.

Similarly there is very little information from African countries on benzodiazepine use and abuse. Earlier publications, scanty as they may be, have been reviewed in the 1982 Impact Study. In a recent report ODEJIDA et. al., (1983) who examined for dependence potential and withdrawal syndrome consequent to benzodiazepine in a general hospital population, was unable conclude whether the symptoms he detected after abrupt cessation of benzodiazepines were a result of dependence on the drug itself or "merely an excerbation of original symptoms of their illnesses."

Apart from data on abuse and dependence, the assessment of public health consequences and social problems associated with the benzodiazepines has still not been achieved. One has to acknowledge that with relative safe substances, the assessment of risks represents a very complex task. Thus, for example, the consequences, both negative and positive, of benzodiazepine use on the job have not been ascertained. Similarly, while there is acknowledged correlation between the use of high doses of benzodiazepines and performance impairment in a test situation, morbidity and mortality statistics are not so decisive with regards to benzodiazepine abuse. Inspite of these lacunae in information, it has to be acknowledged that overuse and abuse of benzodiazepines can induce a degree of individual disfunetionality which could have social consequences. What remains debatable is the extent and degree to which these effects manifest.

3. OPIOID — AGONIST-ANTAGONIST

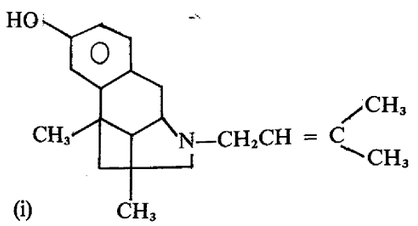
This group of compounds was identified in the search to develop potent analgesic substances without dependence-producing properties. Over the last 2-3 years increasing concern has been expresses by some countries concerning the overuse of these agents which has resulted in reports of abuse and dependence in some of them.

The World Health Organisation conducted a review of this group of compounds in response to a request to review pentazocine, made at the 7th Special Session of the United Nations Commission on Narcotic Drug. They considered five similar compounds - buprenophine, butorphenol, cyclazocine, nalbuphine and pentazocine.

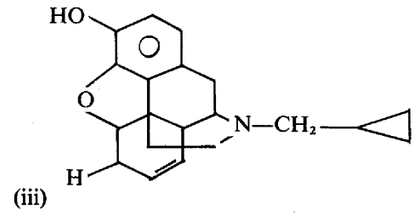
The structures of these compounds are shown in figure 3.1. From a chemical structural viewpoint, all these five compounds are very similar. As a class, they demonstrate both analgesic and narcotic antagonist properties in animals and humans. Whilst there appears to be some quatitative differences in regards to these pharmacological actions, qualitatively they are quite similar. At equivalent analgesic doses they all depress respiration to the same level as morphine; however, unlike morphine, at higher dose ranges, they do not cause increased respiratory depression. In relation to cardiovascular effects, these are generally mild and further there are also quantative differences. In general the acute and chronic toxicities reported for this class are not very significant.

The drugs are rapidly absorbed after parenteral administrative with a half-life varying from about 120 minutes form pentazocine to 240 minutes form buprenorphine. Butorphenol, cyclazocine and pentazocine are excreted mainly in the urine, whereas nalbuphine and buprenorphine are excreted in the faeces. Drug metabolism occurs and the drugs are excreted mainly as conjugates.

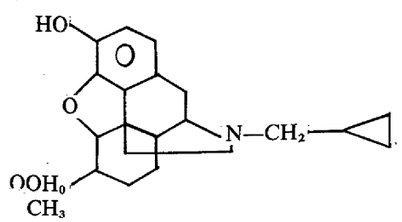
FIGURE 3.1



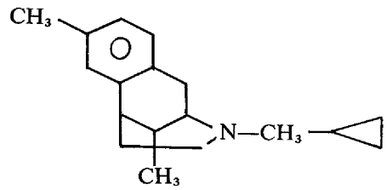
(i) Pentazocine



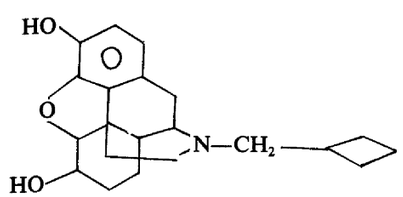
(iii) Butophanol



(ii) Buprenophine



(iv) Cyclazocine



(v) Halbuphine

In respect to *dependence potential* all five drugs precipitate withdrawal symptoms in morpnine dependent rodents and dogs. None of the five compounds suppress withdrawal signs in morphine dependent rhesus monkeys. However, all of these drugs, except for buprenorphine, produce physical dependence when administered repeatedly. However, not only the nature of withdrawal signs differed from morphine, but also the intensity was significantly less. Withdrawal signs was the most significant with butorphenol though less severe than codeine. The reinforcing effects of all these drugs except cyclazocine, has been clearly demonstrated in monkeys, rats and baboons. It may be said that all these drugs, in general, have a dependence potential, but quantitatively it is less than that of codeine.

Human studies have demonstrated that all five compounds are efficacious in relieving pain. In human volunteers analgesic therapeutic doses of these agonist/antagonist drugs depress the respiratory response to carbon dioxide to equal degrees. Reviewing the various human studies it would appear that all these compounds, except cyclozocine was able to produce a state of dependence as well as induce Centrel Nervous System stimulation and depression which resulted in hallucinations, disturbances in motor function and changes in mood. hence fulfilling the requirement of Article 2, Para 4(a).

PENTAZOCINE

(i) Pharmacology

Pentazocine is one of the pioneer opioid agonist/antagonist compounds. In terms of analgesic action, it is approximately ¼ as potent orally as parenterally. The duration of analgesia may sometimes be less than that of morphine (PDR 1981). Analgesia usually occurs within 15 to 20 minutes after intramuscular or substaneous injection and within 2 to 3 minutes after intravenous injection. Pentazocine also weakly antagonizes the analgesic effects of morphine, meperidine and phenazocine (PDR 1982). Further, it causes an incomplete reversal of cardiovascular, respiratory and behavioural depression induced by morphine. However it has sedative properties.

Pentazocine clearly has mixed properties. It has been shown that in morphine dependent dogs, pentazocine resembled nalorphine by being unable to suppress abstinence. Pentazocine obviously has strong nalorphine-like agonistic-effects as well as possessing substantial analgesic properties. The finding that pentazocine is able to precipitate morphine abstinence can be taken to indicates that it antagonises vmorphine-like action.

Reviewing from an abuse liability viewpoint, the results of self-administration studies with pentazocine seem to indicate that it would sustain drug-taking behaviour in experimental animals. However available data shows that pentazocine was less reinforcing than heroin, codeine of dextropropoxyphene when tested in a progressive ration paradigm.

Human studies have demonstrated that pentazocine resembles morphine at low doses but nalorphine-like activity at higher doses. With frequent and repeated use, tolerance develops to the analgesic effect of the drugs. Therapeutic analgesic doses of pentazocine produced a morphine-like euphoria (MBG Scale Evaluation) without the sedative scores (PCAG Scales) or psychotomimetic (LSD Scale scenes) effects. However larger doses were nalorphine-like with dysphoria and no euphoria but with sedation and psychotomimetic effects. Following chronic administration of 60 to 90mg pentazocine given hourly, post-addicts developed a form of physical dependence that can be demonstrated by abrupt withdrawal of the drug of precipitated by nalorphine. This ability to produce dysphoria at high doses makes pentazocine unattractive as a drug of abuse on its own.

Hence with regards to fulfilling the requirements of Article 2, para 4a(i) of the 1971 Convention on Psychotropic Substances, the scientific and medical evidence would support the position that pentazocine has the capacity to produce

(i) a state of dependence

(ii) Central Nervous System stimulation and depression, resulting in hallucinations, disturbances in motor function and mood

(ii) Social and Public Health Issues

Pentazocine is available for sale in 127 countries and it is estimated that since 1977, when it was introduced, about 80 million patients have received more than 800 million parenteral doses. Consumption data for pentazocine is very inadequate. Data from the United States of America shows that therapeutic use was at the highest in 1973 with 6 million prescriptions but the level dropped to 3.5 million for 1980. For the two year period 1981-1982, in Western Europe 119 million doses were administered. Data gathered through the IMPACT study showed that only four countries were able to give consumption data (Table 3.1). From the data one sees that the consumption levels in Australia have gradually reduced from 106.52kg to 1977 to 66.58kg in 1981. One the other hand both Hong Kong and Philippines show increasing levels of use. In Hong Kong the level of consumption

doubled between 1979 and 1980. However it must be stressed that one cannot make any significant inferences based on the limited data available.

Reviewing the information on behavioural toxicities, it has been shown conclusively that central nervous system disturbances occured throughout a wide dosage range, however psychotomimetic side effects were definately dose-related with respect to the parenteral route of administration. No data was available on the dose-related effects after oral use. However most studies put the level of incidence of perceptual disturbances at below 10%. It should be emphasised that the problem of hallucinations/perceptual disturbances was not limited to pentazocine, but it also occurred with other analgesics. Another issue that should be raised here, is that, there are several reports of complicated behavioural manifestation as a consequence to non-medical use of pentazocine, however in nearly all these cases, there has been simultaneous use of tripelennamine and hence one cannot attribute these toxicities solely to pentazocine.

Abuse Liability and Actual Abuse

Pentazocine was initially introduced as a non-dependence producing drug, however quite early reports on its abuse began emerging. Hence, the scientific and medical community have been aware of the possibility of physical dependence occurring with protracted use of high doses.

The early reports on its abuse were limited to reports describing one or two cases. INCIARDI and CHAMBER (1971) systemmatically investigated the nature and extent of pentazocine abuse in three groups of narcotic addicts. They reported that out of one thousand five hundred subjects reviewed, less than 1% had become dependent as a consequence. KANE and POLEKORNY (1975) after an extensive literature search were only able to record 197 cases up to that date. Of this only six cases were related to the oral use of the drug. The abstinence symptoms reported were considered to be mild.

There have been only a few reports of pentazocine abuse outside the U.S.A. Within the United States there is quite extensive epidemiological data on its non-medical use.

The Drug Abuse Warning Network (DAWN) of the U.S.A. generates probably the most comprehensive information from emergency rooms. The data presented in Table 3.2 shows that only 157 mentions were reported in 1975, however there was gradual but steady increase until 1981 when it peaked with 1797 mentions, however since than a decrease in the number of mentions were noted.

TABLE 3.1
Consumption Data for Pentazocine from 1977-1981

Year	1977 (kg)	1978 (kg)	1979 (kg)	1980 (kg)	1981 (kg)
Hong Kong		64	7	131.8	
Malaysia				5.66	6.010
Philippines	35	24.0	56.0		
Australia	106.518	93.911	94.595	79.024	66.584

Further, from Table 3.2, it would appear that pentazocine mentions are not universal within the United States, but clearly occur in localised pockets such as Chicago, New Orleans etc. Figure 4.2 is a graphical representation of the 1981 - June 1983 mention on a quarterly basis (3 monthly). From it one can clearly see that there is a downward trend.

TABLE 3.2
DAWN Mentions
Pentazocine (Totals)

	1975	1976	1977	1979	1979	1980	1981	1982	1983 (1st Qtr.)
Chicago, Illinois	81	190	313	542	416	363	307	203	150
New Orleans. Louisana	5	2	3	54	262	266	634	602	202
Detroit, Michigan	61	30	49	56	110	319	341	254	100
St. Louis, Missouri	NA	NA	NA	NA	93	137	147	161	55
Buffalo, New York	NA	67	67	57	57	46	66	NA	NA
Cleveland, Ohio	10	17	18	17	36	73	212	227	79
Total	157	306	450	726	974	1204	1797	1244	676

The DAWN system also collects data from Medical Examiners on drug induced or drug related deaths. Table 3.3 provides the information available for the period 1977 to 1981 the partial data for 1982. The data shows that from 1978 to 1981 there has been a gradual increase in pentazocine related deaths. A very important finding noted was that the increase in pentazocine-related death as demonstrated by this data was not, in real terms, attributable to pentazocine alone, since the majority of mentioned in fact involved a combination of drugs. For the period under consideration, out of 437 pentazocine associated deaths, 279 mentions had complete analytical results. It was noted that only 54 mentions or 19.4% were directly attributed to pentazocine alone. The 80.6% resulted from the use of a combination of drugs, only one of which was pentazocine. Canton is advocated in the interpretation of the "drug-related homicides" data which accounts for nearly half of the mentions for 1981 and 1982. This data represent primary "gangster-types" who may be drug dealers or other criminals. Whilst pentazocine was not the cause of death for these individuals, their death was a result of some form of violent activity e.g. gunshot, stabbing etc., whenever pentazocine was found in their possession.

Due to the reported deficiencies in the DAWN system such as mentioned may involve one or several drugs and some of these drugs reported in the mention may be totally unrelated to the medical crisis; the inability to identify patients which means a single client may represent one or several mentions; at best allows one only to use the data as a trend index. However, due to the paucity of information, it has to be considered as a prime source for this report.

The National Survey of Drug Abuse, U.S.A. is another data source that was considered. This survey gives an indication of the prevalence of drug abuse in household populations. The 1979 report showed that in the survey out of a total of 7,224 respondents 26 pentazocine abusers were identified. This represents approximately a prevalence rate in the study sample of 0.36% or 360/100,000 persons.

TABLE 3.3
Pentazocine Induced and Related Deaths Reported to DAWN bv the Medical Examiners

	1977	1978	1979	1980	1981	1982*
Drug induced/related deaths	**65**	**38**	**32**	**65**	**59**	**29**
Pentazocine alone	14	8	10	14	NA	NA
In combination with other drugs	51	30	22	52	NA	NA
Drug related homicides	**15**	**10**	**21**	**30**	**44**	**25**
Pentazocine alone	5	0	1	2	NA	NA
In combination with other drugs	10	10	20	28	NA	NA
Drug induced homocides	**0**	**1**	**0**	**1**	**1**	**0**
Pentazocine in combination with other drugs	0	1	0	1	NA	NA
Total number of deaths	**80**	**49**	**53**	**97**	**104**	**54**

* Incomplete data
Sources: DAWN Medical Examinations - 26 MSA's

Illicit Traffic

Illicit use is normally associated with illicit availability which normally arises through diversions of licit drugs or through illicit traffic or both.

Eighteen countries reported the existence of illicit traffic with pentazocine. With the exception of the African continent the countries that reported existence of illicit traffic were scattered throughout the globe. Table 3.4 provides comprehensive information on the illicit traffic and abuse data.

Out of the eighteen countries that reported existence of illicit traffic, seventeen countries also indicated that seizures had been made of pentazocine by their respective enforcement agencies.

TABLE 3.4

Country	Marketted	Existance of Illicit Traffic	Seizures	Existence of Abuse
Australia	x	x	x	x
Argentina	x	x	x	
Austria	x	x	x	x
Belgium	x			x
Canada	x	x	x	x
China (Republic)	x	x	x	
Denmark	x			x
El Salvador	x			x
France	x	x		
German Fed. Rep.	x	x	x	x
Honduras	x			x
Hong Kong	x		x	
Finland	x	x	x	
Italy	x	x	x	
Japan	x	x	x	
Kuwait	x	x	x	
Norway	x	x	x	x
Philippines	x	x	x	x
Poland	x	x	x	x
Portugal	x	x	x	x
Spain	x	x	x	x
Thailand	x			x
U.K.	x	x	x	x
U.S.A.	x	x		x

Table 3.5(a) and (b) provides an analysis by country the number of seizures and quantities seized for the period 1981 and 1982. It can be seen from the data that several countries were unable to quantify their seizures. Further, those countries that had seizure information provided them not only in dosage units but also some in weight/ampoules etc., hence it was difficult to conduct any careful analysis. The general conclusion that could be reached was that the quantities seized varied from insignificant amounts to somewhat large interceptions - 488,014 dosage units in U.S.A. and also that the existence of the traffic was a worldwide occurrency in respect to distribution. However the overall quantities detected outside the United States was relatively small.

TABLE 3.5(a)
Seizures

Country	Before 1981	Seizures on illicit market 1981	Seizures on illicit market 1982	Quantity Seized
Argentina			3 Seizures Oty not given	Substances encountered in form of ampoules of brand name SOSEGON
Australia		3 amp	301 tab. 70 amp	
Austria			200 du seized (fig. of seizures not given)	Substances encouning the form of tablets of brand name FORTRAL
Canada	1063 tabs 338,350 Talwin[R] tablets (14,000ml's of injectable drug)	1411 dose unit + 331.5grs + 65 mls (nos of seizures not given)	Figure not yet	
Federal Republic of Germany		As Fortral[R]: 20 tab; 48 amp; 25 suppositories	Seizures made but figure not available	Offences investigated relating to deversion 1981:- 228 cases 1982:- 259 cases
Finland			1 Seizure 48 dosage units	Substances encountered in form of tab of brand name FORTRALIN
Italy			A few seizures made (no number given) minor quantities	In all cases where this substance had been encountered on the illicit market, it has been in the form of tab with trade name TALWIN

(cont.)

Country	Before	Seizures on illicit market 1981	Seizures on illicit market 1982	Quantity Seized
Norway		1 seizure small quantities only	5 seizures small quantities only	Substances encountered in form of tablets of trade name FORTRALIN
Portugal		3 seizures 20 d.u.	11 seizures 197 d.u.	Substances encountered in forms of tabs and and amp of brand name SOSEGON
Spain		1729 d.u. seized (No. of seizures not given)	9 seizures 153 d.u.	Substances encountered in form of preparations of brand name SOSEGON & pentazocine tides
Kuwait			1 seizure Qty not given	Encountered in form of tablets (trade neme not given)
Hong Kong		7 seizures 106 d.u.	22 seizures 549 d.u.	Substances encountered in forms of tabs & amp. of brand name TALWIN
Japan			6 seizures 149 d.u.	
Philippines		1 seizure 153 d.u.	3 seizures 20 d.u.	In all cases this substance has been encountered in the form of tablets and/ or amp with trade name SOSEGON
Republic of China		7 seizures 9 kg. 910gms 16041 d.u. (injectable)	3 seizures 47,968 d.u. (injectable)	

TABLE 3.5(b)
Thefts of Pentazocine Reported to DEA by DEA Registrants Throughout the US

Period Covered	June 1979-Dec 1980 (19 months)	July 1981-June 1982 (12 months)
Number of Thefts	1,108(58/months)	669(55/months)
Number of Dosage Units		
Talvin 50	435,074	488,014
Talvin Compound	32,901	NA
Talvin Injectable (ml)	43,290	NA

Actual Abuse

Again based on the total data base available to the study it was found that, as shown in Table 3.4, a total of sixteen countries reported that they were aware of the abuse of pentazocine within their countries.

Of these sixteen countries, apart from the United States which had extensive records of abuse, only seven other countries could provide hard data on pentazocine abusers. Table 4(vi) in the Annex provides the relevent data. For 1981 and 1982, the available data showed that 767 persons have been detected form pentazocine abuse outside the United States. Canada reports the presence of illicit traffic as well as abuse. Whilst the true extent is not known, reports show that about 33 cases were identified in 1981. Federal Republic of Germany seems to be

experiencing some pentazocine abuse, but the level of abuse is extremely small in comparison to heroin abuse. Japan also has detected sporadic cases of pentazocine abusers.

Again, the data available outside the United States is extremely poor to allow a global conclusion to be reached. It is obvious that there are scattered reports of actual abuse cases with pentazocine from around the world. However, in real numbers the total number of reports are extremely small when compared to other controlled substances. Furthermore, there are reports on pentazocine abuse from Argentina, Austria, Italy, Spain and Kuwait but there is no published data or reports on the exact extent of abuse, hence it is difficult to determine the severity of the problem.

In conclusion it is clear that pentazocine has the capacity to produce a state of dependence and does cause changes in the central nervous system to an extent that alterations in moods etc. occurs. Further, it is clear that there exists illict traffic for this substance and that it is abused. However with the exception of the United States, there is inadequate data to conclude the pentazocine abuse had reaced significant levels globally.

4. LEGAL IMPLICATIONS OF SCHEDULING PSYCHOACTIVE SUBSTANCES IN THE 1971 COMVENTION

SUMMARY OF THE 1982 IMPACT STUDY

The major aims of the Psychotropic Convention are to restrict the use of psychotropic substances to medical and scientific purposes through a system of co-ordinated national and international measures. Simultaneously here, underlies the objective of the Convention whieh is to minimize the availability of these substances for abuse without unduly restricting them and their availability for legitimate therapeutic purposes. This is a basic difference with the 1961 Single Convention on Narcotic Drugs.

The problems of scheduling criteria and terminology are the result of a discrepancy between the terminology of the Conventions and of both medical and pharmaceutical literature. The Convention does not adequately present scientific criteria of classification for different dependence types nor do they clearly draw the lines between the misuse, abuse or dependence of drugs. Consequently if control is to be international in nature rather than national, then it would be important to clarify these definitions. Furthermore, the 1971 Convention does not address the problem of drug overuse by inadequate prescriptions. As such, it has been recognised by many nations the need for control of psychoactive substances. The legislation against drug abuse as well as the implementation of appropriate measures against it must fit within the general framework of national public health policy thus falling in the sphere of national sovereignity respectively.

The 1971 Convention takes into account the balance of social benefits, social and medical coast and the cost of legislation which is a major advance over previous international legislation. This brought about the advantage (ideally) of a shared responsibility for the international solution of a difficult problem on joining the Convention; as international treaties offer the potential for strenghtening national legislation. However, it was noted that the Convention does not envisage the problems of imitations and counterfeits and its affect on street level abuse.

UPDATE — 1983 IMPACT STUDY

Recent publications have given further support to several conclusions reached in the 1982 Impact Study.

An international working group of experts was convened by the International Council for Alcohol and Addictions (ICCA) and met on October 10-15, 1982, in Tangiers, Morocco. They discussed possibilities of developing "a simplified and concise international control system for narcotic drugs and psychotropic substances" (Biblio-25).

They took into consideration existing and possible contradictions between the two International Conventions and expanded on some conclusions reached by a similar working group in Toronto 1980 (Biblio-28). In view of the significant value some important points from the Tangiers Meeting are highlighted here.

BAYER (Hungary) stated: "The compromise between the interests of developed and developing countries does not work: there are doubts about the functioning of the export declaration system for Schedule III substances and the export declaration system does not exist at all for Schedule IV. The monitoring of international trade in these substances is impossible, consequently nobody is in a position to check the respect of an import prohibition under Article 13 by a country."

BAYER also suggested a new calssification for narcotic and psychotropic drugs whereby most Schedule III and IV substances were excluded. He proposed to establish a comprehensive "WHO Warning List" containing substances not under international control and suggested that the hypno-sedatives, tranquillizers, anti-parkinson drugs and antihistamines which are currently listed in Shedule III and IV or are being considered for international control should be put in this separate list.

Similarly, GOTHOSKAR (1982) (India) emphasized that the 1971 Convention "aims at effective control measures at the international level over substances in Shedule I and II only, and not over substances in Schedules III and IV." He called for a rationalisation in international drug control and proposed 4 newly defined schedules containing substances presently controlled in Schedule IV of the Single Convention and Schedules I and II of the 1971 Convention, but excluding substances presently controlled in Schedules III and IV of the 1971 Convention from international control measures.

HUYGHE (Belgium) (1982) outlined some possible solutions. As alternatives to international control measures he put forward the need "to create a drug monitoring system designed to monitor the substance and to immediately spot possible tendencies towards abuse." Further "information to members of the medical and pharmaceutical professions" as well as "information to and health education of the public" were mentioned as

means to limit the use of all these substances to medical and scientific purposes.

One of the questions concerning the 1971 Convention is to what extent it can help countries in their drug abuse problems. ANUMONYE (1981) (Nigeria) has opined in the Toronto Session, that ratifying the Convention "would transfer the responsibility of enforcing the Convention on to the world body which would have the administrative machinery to carry this out" (Biblio-1). However, it should be pointed out from a legal perspective that the 1971 Convention is not self-executing. This means that the Convention needs transformation into national legislation, formalisation at the national level and implementation of these national rules. The way the Convention is phrased leaves a large scope of discretion to the national legislator. Therefore, joining the Convention has no effect on drug abuse control, unless a country enacts and implements appropriate national legislation. International control does not stand by itself. Before substances are considered for international control, it should be checked whether a problem existing with such substances and if it cannot be effectively dealt with at the national level.

SCHROEDER (Germany) stressed in a recent publication (Biblio-27) that one of the major problems for countries with extensive pharmaceutical industries is how to integrate into their national law, preparations containing substances listed in Schedules III and IV of the 1971 Convention; applying the Convention to these substances requires a considerable amount of work for member states and for the international authorities involved in its implementation. Approximately 400 preparations containing substances listed in Schedules III and IV were reported to be on their market.

GAMEZ (Philippines) reported (Biblio-9) difficulties to adapt their national legislation to the international Conventions. He concluded that "ultimately the public suffers from the law that was intended to protect it." Furthermore he reported the results of a survey on regulated drugs; this showed that only 12% of the pharmacists would definitely continue to order and retail regulated drugs as a matter of service; 26% would probably and 62% would definitely discontinue to order regulated drugs. Among the reasons given for this negative attitude were "too much paper work, recording, reporting, keeping inventory" and "frequent inspections by different inspectors".

The regulatory perspectives with regard to benzodiazepines in the United States have been discussed upon in a recent paper by TOCUS (1983) et. al., (Biblio-31). It was stressed that all benzodiazepines currently marketed in the US are submitted to the same national control status as there is insufficient evidence to differentiate between them as to their abuse potential. The benefit/risk ratio for the class of benzodiazepines as a whole was considered to be favorable.

Regarding the implementation, D.M. SMITH (Canada) stated in Tangiers (Biblio-30) that "the big problem is not so much the legitimate control of drugs, which is moderately well under control by the international treaties, but the illicit traffic in the drugs, and here the treaties have gone about as far as they can. Parties to the treaties presumably have enacted, as sovereign nation-states, the appropriate legislation to apply on their territories the necessary constraints on the illicit traffic. The difficulty comes with the enforement of this legislation, due to a variety of reasons, mainly a lack of resources for this effort, and other economic and social difficulties."

In summary, most of the questions raised pertaining to legislatory matters in the previous Impact Study remain unanswered. Serious doubts continue to exist with regard to the effectiveness of international control and its impact at the national level. The question can be put as follow: either effective national control exists and is implemented, then international control - taking into account the weakness and inconsistencies of Schedules III and IV of the Convention - can contribute to a limited extent, to solve national problems; or in the event that the national control mechanisms do not work properly, then international control has little to contribute. Alternatives to international control measures should therefore be considered, e.g. monitoring of the specific situation and exchange of information between the member states, proper information of physicians, pharmacists and health care workers as well as improved health education of the patients and the general public. Such measures can be seen not only as substitutes to control but also as concurrent activities.

5. ASSESSMENT OF IMPACT OF SCHEDULING

Summary of The 1982 Study

The Impact Study 1982 reflected on the criteria that needed to be examined and fulfilled before any substance can be scheduled under the 1971 Convention. It was further noted that many countries had expressed concern over the past few years about the effectiveness of the 1971 Convention. This was borne out by the results of the inquiry that formed the basis of the 1982 Impact Study. Nine out of 11 countries that had answered the questionnaire have opined that their existing problems caused by psychotropic and other psychoactive substances[1]. Deficiencies in information gathering and in drug monitoring, inadequate resources to implement the 1971 Convention properly and the means to implement record keeping and inspection procedures, were reported, even if these mechanisms had been created by legislation.

Only three of the eleven countries felt that international control would help them in solving their problems with psychoactive substances. The eight countries that felt that international control would have little or no effect on their national psychoactive drug problems gave among others the following reasons:

The existing national controls were considered adequate and in most instances more stringent than the control measures called for by the 1971 Convention. Furthermore, if international control was stringent at the level of schedules 1 and 2, schedules 3 and 4 had little if any impact, and it was opined that the 1971 Convention was unable to address the main problem of illicit traffic. Misuse and illegal availability of therapeutically used substances seemed to stem in part from diversion and from bad prescribing practices of a minority of physicians. There problems were considered to be best dealt with at a national level through law enforcement and through physicians' education. For several countries the main problem with psychotropic substances and other psychoactive drugs was sometimes closely related to the illegal availability and to the existence of counterfeit products which could not be controlled by the 1971 Convention.

The potential impact of scheduling benzodiazepines in the 1971 Convention was a special raised in the 1982 Impact Study questionnaire. The rather general consensus of the countries that had answered the questionnaire may appear to be that since banzodiazepines were alredy controlled nationally as prescription drugs, international control would not in any way significantly enhance control measures. All authorities acknowledged that the benzodiazepines, if left totally uncontrolled, did have the potential to cause an abuse problem; however it was emphasised that national control was the best and most appropriate mechanism for controlling a group of substances which had wide therapeutic use and did not, in their view, constitute a global problem.

Update — 1983 Study

5.(a) Introduction

The objectives of the first (1982) Impact Study were to develop and apply data gathering methodologies to obtain and assess relevant information on substances which the UNCND might usefully consider in fulfilling its functions on the question of scheduling drugs for international control. In concluding the researchers had recommended that the developed procedure should be applied to all future psychoactive substances being considered for scheduling.

During the debates of the UNCND on the subject of international control of drugs, several delegations indicated the usefulness of this study. Further some individual members suggested that it would be valuable if the assessment procedure developed could be refined and utilised on other substances as well as other countries, particularly from Africa.

The next group of substances that were being reviewed by the World Health Organisation (WHO) were the narcotic mixed agonist-antagonist and it was intended to apply this assessment procedure to this group. However, before the study could be initiated two critical decisions were reached which changed the configeration of the study. *Firstly,* the UNCND at the 30th Session decided not to schedule the benzodiazepines and by Resolution 4(XXX) through which WHO was requested to "(a) urgently review and assess, as part of its regular function under the Convention on Psychotropic Substances, all benzodiazepines currently on the market as of a specific date to be determined by that Organization, (b) undertake as soon as possible the review and assessment of amphetamine type stimulant substances and of barbiturates and non-barbiturate sedative-hypnotics, (c) con-

[1]*"Psychotropic substances" means substances listed in the 1971 Convention. "Psychoactive substances" designates all CNS-active substances, whether scheduled or not scheduled in the Convention.

tinue to use the procedures as stated in resolution 2(S-VII), paragraph 5 in conducting this review and assessment, (d) make available its findings and recommendations, on a substance by substance basis, as well as its sources of information and appropriate background documents to the Secretary-General as requested in resolution 2(S-VII), paragraph 7; *Secondly,* the WHO Advisory Committee established to review drugs for international control met in March 1983, and decided to recommend only pentazocine for control under Schedule III of the 1971 Convention on Psychotropic Substances. In view of these decisions the research team decided to collect data on "al marketed banzodiazepines as determined by WHO" and on pentazocine. Further, as suggested, two countries were selected from Africa, an additional European country as well as all those countries that had previously participated in the first study.

The original questionnaire was modified, in accordance with comments received from various colborators.

The survey instrument, as designed, was aimed at eliciting information on:

(i) The adequacies and/or inadequacies of national controls in the various countries;

(ii) The effect of scheduling drugs under the 1971 Convention o the related drug abuse problem.

Specific information was also gathered on:

(i) The extent of drug abuse including benzodiazepine and pentazocine abuse;

(ii) The effect ot national (legislative) control on the legal and illegal availability of benzodiazepines within the various countries;

(iii) The impact of international control.

Methodology

The survey instrument designed for the 1982 study was reviewed and modified in accordance with the comments received from collaboraters as well as on the experience gained. The modified questionnaire was circulated to the UNDND and WHO for comments and the final version was available in English and French languages. The additional countries chosen were Senegal (for Africa) and Norway (for Europe). The 17 countries to whom the questionnaires were circulated, were representative of the countries reporting verying degrees of problems related to the abuse of psychotropic and narcotic drugs.

In this section of the report we have focused on issues relating to the economic, social, legal and administrative aspects. Data generated on other aspects, such as illicit traffic, extent of abuse, etc. have been dealt with in other parts of this report. For the sake of conciseness, we have had to condense/summarise the various responses provided by participating countries. Further we have considered responses from the 1982 study as part of the data base with the relevant update provided and also included data from the countries participating for the first time in this follow-up study.

Results

At the time of the first Impact Study in 1982, fifteen countries were invited to participate, of which eleven completed the necessary questionnaire. In this follow-up study, the sample was expanded to seventeen countries and fourteen countries responded. Thus the combined data base represented sixteen countries, (participating countries are underlined).

1982 Countries	**1983 Countries**
Australia	*Australia*
Burma	*Burma*
Canada	*Canada*
Federal Republic of Germany	Federal Republic of Germany
Hong Kong	*Hong Kong*
India	*India*
Indonesia	Indonesia
Malaysia	*Malaysia*
New Zealand	*New Zealand*
Nigeria	*Nigeria*
Pakistan	*Norway*
Philippines	*Paskistan*
Singapore	*Philippines*
Thailand	*Senegal*
United States of America	*Singapore*
	Thailand
	United States of America

Of the 16 countries, 10 are signatories to the 1971 Convention, whilst the rest have not acceded to it.

5.(b) Impact of the 1971 Convention

Disadvantages/Weaknesses

In general, with regards to the implementation of the 1971 Convention, the non-signatory countries enumerated greater number of difficulties than the signatory nations. Several problems or disadvantages of the 1971 Convention were reported.

The need to institute additional administrative procedures at the national level and the consequent financial costs associated with complying with the Provisions of the Convention was raised. Some countries queried to the cost-benefit aspects of controlling therapeutic agents especially since they felt that the 1971 Convention was inadequate as a control instrument.

Non-signatory countries raised the issue that, in the context of their countries, some of the provisions of the Conventions were incompatible with their national laws. Canada also pointed out that the current procedure to enable countries to become signatories with reservation was cumbersome since such conditional assent had to have the concurrence of other parties to the 1971 Convention.

The lack of detailed criteria for the inclusion of substances in the 1971 Convention as well as with regards to exemption was pointed out. India expressed concern that signatories were required to exercise strict control measures, in some instances, for psychotropic substances for which there was no national reports of abuse and which were considered essential drugs within their context. Phenobarbitone was cited as an example for which it was opined that in should not be controlled under the 1971 Convention.

Some developing nations expressed strong concern about the current inadequacies of the 1971 Convention. It was reported that, at present, apart from substances in Schedules I and II of the 1971 Convention, there was, in reality, no international co-operation in the control of exports of unwanted psychotropic substances to their respective countries; the only recourse open to them was to apply Article 13.

Nigeria pointed out that Article 12 (2c) which covers substances under Schedule III of the 1971 Convention, because of the long time gap allowed (ninety days) between the actual exportation and the dispatch of the declaration of export to the recipient country, gave room for illicit importation/reexportation to continue.

It is appropriate to point out here that the opinions noted here have also been stressed by drug controllers attending the meeting on the 1971 Convention held in Tangiers 1982 (see preceding chapter).

Further Nigeria also opined that with regards to the mechanism of decision to include or remove a substance from international control as outlined in Article 17(2) should be amended so that decision can be reached by a simple majority vote.

Benefits/Advantages

Inspite of the criticisms made of the 1971 Convention a large number of countries reported that the 1971 Convention was beneficial and supportive to their drug control efforts.

There was concensus that the 1971 Convention acted as a basis for some countries to structure their national drug control legislations where such legislation is absent or inadequate. Further it generated indirect pressure for national legislative bodies and enforcement agencies to comply with the Provisions of the 1971 Convention. Australia noted that this element was important, especially in their context, wherever Federal legislations were not applicable.

Nigeria pointed out that the 1971 Convention had been established to facilitate global action against the abuse of psychotropic substances without curbing their availability for legitimate use. Australia noted that the acceptance of particular control measures including the regulations and documentations associated with the import and export by parties, facilitated licit trade whilst ensuring national interest such as minimising illicit diversions ect. They also reported that the 1971 Convention provided an appropriate and effective method for advising importer/exporter countries of their particular national requirements. They cited that the prohibition of imports of methaqualone into Australia as an example of effective control of a substance under Schedule II of the 1971 Convention.

Canada, Thailand and Senegal supported the view that scheduling a substance under the 1971 Convention facilitated their respective nations to prevent the import of these substances of abuse.

Canada and Senegal also felt that the 1971 Convention facilitated not only the gathering of statistical information on production, export, import and sales of the controlled substances but also intelligence information. Several countries indicated that the listing of substances under the 1971 Convention drew the attention of countries to the abuse liability, and hence stimulated stricter control over manufacturing import and sale of these substances. India noted that as a result of strict regulatory measures there was a trend towards decreased consumption which was considered as a positive effect for dependence producing substances.

It was clear from the replies received from the participating countries, that in general the advantages of international control through the 1971 Convention were reported to our weigh the disadvantages.

All countries participating in the study had legislative measures for the control of psychoactive substance. In nearly all the countries studied, psychotropic and other psychoactive substances used in therapy were available only on prescription. Further, whilst countries had national controls for the importation and re-exportation of these substances, some felt that these were not totally adequate. All countries indicated that, in principle, they had the necessary procedures for monitoring/record keeping and inspection, but a few of them emphasised that they experienced difficulties in relation to its implementation (e.g. Canada, Pakistan, Malaysia, Senegal).

In responding to the inquiry whether international control would assist them in dealing with their respective national problems associated with psychoactive substance abuse, only eight countries replied affirmatively. Those countries which opined that international control did not enhance national control, unanimously believed that the current level of national control for those substances listed under the 1971 Convention were adequate and in many instances were more stringent than those measures provided for under the Convention. India also reported that, in their context, many of the psychoactive substances for which reports of abuse have been received, were manufactured within athe country and only a small percentage was imported. As such international control, in their context, was not very helpful.

The countries that opined that international control was beneficial and facilitated national control, could be categorised as being "developing nations." They supported their position by stating that international control facilitated the automatic listing of these substances which were liable for abuse under their national gerulations hence immediately enhancing control. They added that international control also provided their drug control authorities with supportive powers to monitor/control the importation, (re) exportation and utilization of these substances. Another important point raised was the listing of substances under the 1971 Convention, which not only quickly drew the attention of national governments and drug control agencies, but also alerted the medical practitioners to the potential dangers consequent to indiscriminate use.

5.(c) Potential Impact of Scheduling Substances for International Control

(i) Benzodiazepines

Reviewing the current national control status, nearly all the countires, with the exception of three reported that benzodiazepines were available only on medical prescription. Nigeria pointed out that at present these substances were controlled by administrative procedures, however a proposed legislation on its control was awaited. In several of the participating countries, the purchase and use without medical supervision is considered an offence under their national laws. In nearly all countries studied, the importation and distribution of these substances were restricted to pharmacists or duly authorised agents. A few countries require the maintanance of sales records.

Some countries reported that they had imposed additional, more stringent, control measures on those benzodiazepines, or benzodiazepine preparations that were being reported as being abused. Singapore, Malaysia, Philippines and Thailand had placed one or two benzodiazepines under the Misuse of Drugs Act/Dangerous Drugs Act. Information available from these countries indicate that by listing these psychoactive substances under the Misuse of Drugs Act/Dangerous Drugs Act, illegal availability had been significantly reduced. Further it was reported that legal use also had reduced. This reduction was clearly due to the enhanced legislative enforcement powers as well as stricter control on legal use. The data also showed that particularly with the benzodiazepines, stringent control of a single or few banzodiazepines caused some illegal users to turn to other types of benzodiazepines. Medical practitioners also changed their choice, to avoid the additional record keeping burden. The experiences in these countries would lend support for a more global or group approach in deciding on control for substances that have very similar activities.

In general, all countries reported that, under the current legislative measures, the legal availability of benzodiazepines at hospitals and in medical practice were not hampered. With regards to illicit availability and use, the participating countries were confident that their national control measures were adequate to prevent the

diversion of legitimately imported benzodiazepines. Several countries, particularly from South-East Asia and Africa reported severe difficulties stemming from the illegal importation and consequent illegal availability of benzodiazepines. These countries *reiterated* that often these substances were brought into their countries by deliberate mislabelling and were retailed cheaply through unethical outlets.

As in the first Impact Study, the national authorities of the participating countries were asked to assess the effect of placing the benzodiazepines under international control and their consequent impact at the national level. All the participating countries reported that international control of benzodiazepines will not affect legitimate availability for medical use. Nigeria, Thailand and Senegal noted that the inclusion of these substances under the 1971 Convention would increase the level of national control, and they will be treated as available on prescription only. It should be pointed out that the majority of countries consider that international control would have no impact on licit availability because these substances were already controlled as prescription drugs at the national level. With respect to the dispensing of these substances, a few countries noted that international control may be restrictive in that paramedical healthcare workers may not be permitted to dispense them in several countries. It was emphasised that this type of health workers were the backbone of health services in some countries. Some countries however pointed out that differential control of the benzodiazepines at the international level would clearly effect medical practice. Medical practitioners would tend to avoid prescribing those substances and seek alternatives. Philippines expressed concern that such a decision may lead medical prescribers to change to other substitutes which may be more dangerous.

In respect to *illicit availability,* Australia, India, Norway, Singapore opined International Control will have little or on impact. Canada opined their support for any international control that would facilitate the ascertainment of move comprehensive information that would enable indentaification of consumption needs, production output and extent of use and abuse and favour international efforts to reduce illicit traffic in these substances. On the contrary Hong Kong, Nigeria, Senegal, Malaysia and Thailand were of the view that international control would reduce illegal availability that occurs as a consequence to diversion from illicit sources as well as from illegal traffic. Some countries pointed out that the problem of benzodiazepine abuse was underreported and through international control, more comprehensive information can be collected to enable identification of consumption needs, production output and extents of use and abuse. This would enable one to develop appropriate national, regional and international strategies to reduce or prevent the occurence of problems of benzodiazepine abuse.

When inquired whether the benzodiazepines should be sheduled in the 1971 Convention, a vast majority of the countries gave no definite answer. Only four countries (Austria, Belgium, Denmark, and Federal Republic of Germany) stated that they saw no necessity to include benzodiazepines in the 1971 Convention. On the other hand twenty-one countries indicated acceptance and even supported a control decision. However some were not fully convinced of the value of international control.

In relation to control several countries qualified their positions by indicating that a "group approach" was a pre-requisite. Australia "strongly urged that, *should* controls be considered necessary, they be applied to all benzodiazepine as a group." Similarly Sweden pointed out that "no single drug should be singled out as *less* dangerous than the other". Ten other countries (Austria, Malaysia, Nigeria, Pakistan, Panama, Senegal, Switzerland, Thailand, United Kingdom and United States) opined that they favoured a group approach.

(ii) Pentazocine

In all the participating countries pentazocine was strictly controlled through national legislation and were only available as a prescription drug. In several of these countries additional controls had been imposed. In Canada pentazocine is currently included in Schedule C of the Food and Drugs Act and it has been recommended for inclusion in the Schedule of the Narcotics Control Act. In Nigeria and Senegal, a special licence is required for its importation and only pharmacists are allowed to do so. In Norway, it is listed in the Narcotic Drugs Schedule and it is available only on non-repeat prescriptions. In Philippines the importation of pentazocine requires a special import certificate which is approved only by the Dangerous Drugs Board and can be prescribed by physicians possessing a special (opium) license. In Thailand it is treated as a dangerous drug.

A significant majority of the countries indicated that in their opinion pentazocine should be treated as a narcotic drug and hence should be controlled in a similar manner. It was pointed out that uncontrolled use or easy availability would cause a significant abuse problem. Further it was reported that inspite of enhanced national controls in several countries, pentazocine was still availabile for legitimate medical use.

Four countries - Australia, Canada, Philippines and Thailand reported that, inspite of stringent national controls. they had evidence of non-medical use of pentazocine. An increase in the level of non-medical use may in turn stimulate the establishment of an illicit traffic in these substances. With regards to illicit traffic three countries (Australia, Canada and Philippines) reported that there was such in their countries, and similarly Canada, Hong Kong and Philippines acknowledged that pentazocine was illegally available.

Examing the responses received from participating countries on the issue of the effect of placing pentazocine under international control, again every respondent opined that International Control will not affect legal availability for use at hospitals and for medical practice. Several countries pointed out that the current level of national control was stringent and international control would, at best, only facilitate law enforcement activities.

In respect to *illicit availability* Australia, Canada, Philippines and Thailand opined that international control would have impact with respect to illegal availability consequent to illicit traffic. They were unanimous in the opinion that there would be a reduction at the level of ilicit traffic. Several respondents supported the view that International Control would curb the further spread of abuse of pentazocine and hence should be considered as an important preventive measure.

(c) **General Administrative Costs**

It was pointed out that any decision to control a substance internationally will have consequent administration costs to all parties. In general a majority of the participating countries indicated that to bring under international control such a large number of benzodiazepines without doubt would cause significant increases in manpower and administrative costs. New Zealand, Nigeria and Segenal opined that they would be in a position to cope without such additional administrative and manpower needs.

However with pentazocine a lesser number of countries predicted increased administrative and manpower costs. The reason for this was that, at present, a large number of countries already controlled pentazocine as a "narcotic drug" and as such international control would not significantly alter current control requirements.

The argument that seems to emerge is that for pentazocine more countries opined that the benefits of international control outweigh the possible risks that can be generated through uncontrolled availability. Further many feel that pentazocine is not an essential therapeutic agent and that there were several other alternatives. On the contrary, there is more ambivalence towards the scheduling of the benzodiazepine group of substances. Whilst there is clearly stronger evidence of illicit traffic, availability and abuse, many countries felt that their current national controls were adequate to deal with the situation. In general the "developed countries" are more united on the question of the need for control and here several "developed nations" also expressed a similar viewpoint; the difference in opinion emerges only in relation to possible control of a selected number of benzodiazepines. This position seems unacceptable to newer developing nations who envisage several legal, administration and enforcement problems. Above all they seem to be unconvinced that there is *sufficient evidence* to prove a particular benzodiazepine is significantly safer to an extent that it would not have the potential to cause an abuse problem within nations.

BIBLIOGRAPHY

1. Anumonye, A.: The Convention on Psychotropic Substances with Special Reference to Nigeria in SMART, R.G. et. al.: Psychotropic Substances ..... Addiction Research Foundation, Toronto, Canada, 1981.

2. Balter, M.B.: Manheimer, D.I.; Mellinger, G.D.; Uhlenhuth, E.H.: A Cross National Comparison of Anti-Anxiety/Sedative Drug Use presented at the VII World Congress of Psychiatry, Vienna, July 1983 to be published in Current Medical Research and Opinion for Fall 1983.

3. Bayer, I.: Scope and Limits of International Control. Report of a working group on a simplified and concise international control system ..... ICAA, pp. 31-33.

4. Cai Zhi-Ji: report submitted to WHO's 7th Review of Psychotropic Drugs

5. Caplan, R.D. et. al.: Tranquilizer use and well-being: a longitudinal study of social and psychological effects, presented at the Annual American Psychological Association Meeting, August 28, 1983 to be published.

6. Cumin, R. et. al.: Experientia, *38*, 833-834 (1982)

7. Dairman, W.M and Juhasz, L.P.: Pharmacologist *24*, 125 (1982).

8. FDA (USA): letter to US firms marketing benzodiazepines with warning against comparative advertising on the basis of unsubstantiated evidence. Scrip No. 751, December 6th, 1982, page 10.

9. Gamez, G.L.: Drug Control and Regulation in the Philippines - Republic Act 6425 in Report of the Working Group on the Use and Abuse of Psychotropic Substances in Developing Countries With Special Reference To Benzodiazepines. 10-15 Oct., 1982, Tangiers, Morocco ICAA publication, Lausanne. pp. 11-21.

10. Gerald, M.C.: Summary of benzodiazepine consumption in the Americas. Report submitted to the 8th Review of Psychoactive Substances, Geneva, 12-16 September 1983.

11. Gothoskar, S.S.: Scope and Limits of International Control (Scheduling, Exemptions and Role of WHO) in Report of the Working Group ..... on a simplified and concise international control system ..... ICAA, pp. 38-40.

12. Haefely, W.: The Biological Basis of Benzodiazepines Actions. Journal of Psychoactive Drugs 15, 19-39 (1983)

13. Haefely, W. and Cumin, R.: Use of the benzodiazepine antagonists flumazepile (Ro15-1788) in studies of physiological dependence on benzodiazepines. Prescutation at WHO's 8th Review on Psychotropic Substances, Geneva, Sept. 11, 1983.

14. Harvey, J.G.: Deaths From Overdose and Drug Addiction in Central London. Paper presented at the 13th International Institute on the Prevention and Treatment of Drug Dependence, Oslo, Norway, Oct. 10-14, 1983.

15. Huyghe, B.: National Control In the Frame of International Drug Control Feasibility of a Fusion of the Two Conventions in Report of the Working Group on a Simplified and concise international control system .... ICAA, pp. 50-61.

16. Impact Study: See Navaratnam

17. Ladewig, D.: Abuse of benzodiazepines in Western European Society - incidence and prevalence, motives, drug acquisition. Consequences, detection and measures considered, to be published in Pharmacopsychiatria.

18. Ladewig, D.; Banziger, W. and Lowenheck, M.: Tranquillizer Abuse - Results of a Nationwide Swiss Survey, Journal of Drug Research (TNO) *6*, 1131-1137 (1981).

19. Lucas, S.E. and Griffiths, R.R.: Science, *217*, 1161-1163 (1982)

20. McNicholos,L.F. and Martin, W.R.: Life Sciences, *31*, 731-737 (1982).

21. Navaratnam, V.: Impact of scheduling drugs under the 1971 Convention on psychotropic substances the benzodiazepines reappraised. A study funded by the United Nations Fund for Drug Abuse Control. Published by the National Drug Research Centre, Universiti Sains Malaysia, Pulau Pinang, 1982.

22. Nordiska läkemedelsnämnden Nordisk läkemedelgstatistik 1978-1980. Uppsalo 1982. Quoted by Petursson & Lader.

23. Odejide, A.O.; Ohaeri, J.U. Dr. and Bamgbone, E.A., Dr.: Dependence Potential and Withdrawal Syndrome of Benzodiazepines: The Experience in a Nigerian General Hospital. Paper presented at the 13th International Institute on the Prevention & Treatment of Drug Dependence, Oslo, Norway, Oct. 10-14, 1983.

24. Petursson, H. and Lader, M.H.: Pattern and extent of tranquilliser usage. Paper submitted to the 8th Review of Psychoactive Substances, Geneva, 12-16 September 1983.

25. Report of a working group on a simplified and concise international control system for narcotic drugs and psychotropic substances. 10-15 Oct., 1982, Tangiers, Morocco, ICAA publications, Lausanne quoted as "Reported of the working group on a simplified and concise international control system ..... ICAA"

26. Report of 8th Review of Psychotropic Drugs, Geneva, Sept .... 1983.

27. Schroder, O.: The Ratification of the Convention on Psychotropic Substances 1971 and its transposition into national legislation in the Federal Republic of Germany. Bulletin On Narcotics *34*, 1-19 (1982).

28. Smart, R.G.; Murray, G.F.; Archibald, H.D.: Psychotropic Substances and Their International Control. Addiction Research Foundation, Toronto, Canada, 1981.

29. Smith, D.E.: Introduction to A Multidisplinary Forum, The Benzodiazepines, Two Decades of Research and Clinical Experience, Oct. 8-11, 1982, San Francisco. Journal of Psychoactive Drugs, Vol. *15,* Pages 1-7, 1983.

30. Smith, D.M.: General Comments On The Working Paper For An International Working Group On A Few Basic Problems Of International Drug Control - Discussion of A New International Convention On Controlled Substances. Report of a Working Group On A Simplified and Concise International Control System .... ICAA, pp. 62-67.

31. Tocus, E.C.; Nelson, R.C. & Vocci, F.J.: Regulatory Perspectives and The Benzodiazepines Journal of Psychoactive Drugs *15,* 151-157 (1983).

32. United Nations Division of Narcotic Drugs: Benzodiazepines Report for use at the 8th WHO Review of Psychoactive Substances for International Control, Sept. 12-16, 1983.

33. WHO Review Group: Use and abuse of benzodiazepines (based on report of 6th Review). Bulletin of WHO, 61, 551-562 (1983)

34. Woods, J.H., Kat, J.L. and Winger, G.: Abuse and dependence liabilities of benzodiazepines. Submitted in manuscript from the WHO's 6th review, updated version submitted to WHO 8th review to be published.

ANNEX

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	AUSTRALIA					
Drug Type	**1976/77**	**1977/78**	**1978/79**	**1979/80**	**1980/81**	**1981/82**
Alprazolam						
Bromazepam						
Camazepam						
Chlordiazepoxide						
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam	473	412	382	319	295	
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam						
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam						
Nitrazepam	304.5	313.5	277	269		
Nordezepam						
Oxozolam						
Oxazepam	1926	2556	3294	3684	4332	
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	BRAZIL					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam						
Camazepam						
Chlordiazepoxide						
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam						850
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam						
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam						
Nitrazepam						6
Nordezepam						
Oxozolam						
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Comsumption Figures from Various Countries (in kg. unless stated)

Country	BOLIVIA					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam				4000 cap		
Camazepam						
Chlordiazepoxide				36200 tab		
Clobazam						
Clonazepam					10000 tab	
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam				705000 tab 28,500 amp		
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam					5000 tab	
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam						
Nitrazepam				1000 tab		
Nordezepam						
Oxozolam						
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	CYPRUS					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam						
Camazepam						
Chlordiazepoxide				1050 380 tab		
Clobazam						
Clonazepam				37410 tab 10b		
Clotiazepam						
Clorazepate				330 000 tab		
Cloxazolam						
Delorazepam						
Diazepam				4161 585 tab 1833b		
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam				1452 000 tab		
Loprazolam						
Lormetazepam						
Medazepam	N/I	N/I	N/I	177,290 t	N/I	
Nimetazepam						
Nitrazepam				547,920 t		
Nordezepam						
Oxozolam						
Oxazepam				45725 tab		
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam				63000 tab		
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	HONG KONG					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam	NM	NM	1.47	3.37	5.16	3.78
Camazepam						
Chlordiazepoxide		222.6	187.1	517.03	361.6	192.44
Clobazam			5.98	11.2	2.30	3.46
Clonazepam		0.178	0.261	0.330	0.04	0.40
Clotiazepam						
Clorazepate	0.440	1.670	2.470	3.87	3.22	
Cloxazolam						
Delorazepam						
Diazepam		178.87	8.65	221.37	133.3	231.8
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam	NM		0.70	1.58	2.00	1.80
Flurazepam		9.910	9.350	16.820	17.85	13.48
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam	5.770	4.360	8.140	12.77	3.47	
Loprazolam						
Lormetazepam						
Medazepam	2.436	2.133	2.695	4.23	3.75	
Nimetazepam						
Nitrazepam	3.480	1.460	1.200	75.3	1.90	
Nordezepam						
Oxozolam	2.500	4.640	7.860			
Oxazepam	4.208	7.990	6.230	8.04	1.58	
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam	3.876	12.690	3.590			
Temazepam		6.89	3.59	4.97	5.79	
Tofisopam	10.160	6.890	3.590			
Tetrazepam						
Triazolam		0.29	0.33	0.20	1.04	
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	INDONESIA					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam		0.007	0.010	0.013		
Camazepam						
Chlordiazepoxide		0.347	0.528	0.509		
Clobazam						
Clonazepam	NM	NM	NM	NM	NM	
Clotiazepam						
Clorazepate	NM	NM	NM	NM	NM	
Cloxazolam						
Delorazepam						
Diazepam		0.129	0.128	0.116		
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam		0.006	0.833	0.964		
Flurazepam	NM	NM	NM	NM	NM	
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam		0.003	0.004			
Loprazolam						
Lormetazepam						
Medazepam		0.019	0.015	0.013		
Nimetazepam						
Nitrazepam		0.008	0.013	0.016		
Nordezepam						
Oxozolam	NM	NM	NM	NM	NM	
Oxazepam	NM	NM	NM	NM	NM	
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam		0.004	0.003	0.002		
Temazepam		0.004	0.004	0.004		
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	JAMAICA					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam						
Camazepam						
Chlordiazepoxide						
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam						4567000 tab
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						2000000 tab
Lorazepam						
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam						
Nitrazepam						
Nordezepam						
Oxozolam						
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	JAPAN					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam						
Camazepam						
Chlordiazepoxide						
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam		1750	1759			
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam						
Loprazolam						
Lormetazepam						
Medazepam	N/I			N/I	N/I	
Nimetazepam						
Nitrazepam		992	1174			
Nordezepam						
Oxozolam						
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	MALAYSIA					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam		1.509	1.098	0.975	0.529	
Camazepam						
Chlordiazepoxide		24.963	29.122	3.920	1.488	
Clobazam						
Clonazepam		0.395	0.603	0.726	0.469	
Clotiazepam						
Clorazepate			0.75			
Cloxazolam						
Delorazepam						
Diazepam		50.512	39.898	4.579	17.617	
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam		3.430	4.232	5.501	2.53	
Flurazepam		2.012	2.163	2.232	1.425	
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam				1.276		
Loprazolam						
Lormetazepam						
Medazepam		2.017	1.885	1.739	0.845	
Nimetazepam						
Nitrazepam		3.614	3.383	2.168	1.160	
Nordezepam						
Oxozolam	NM	NM	NM	NM	NM	
Oxazepam	NM	NM	NM	NM	NM	
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam				2.345		
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	NEW ZEALAND					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam						
Camazepam						
Chlordiazepoxide						
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam						
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam						
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam						
Nitrazepam						
Nordezepam						
Oxozolam						
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam					200-800g	650-2600g
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	NORWAY					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam						
Camazepam						
Chlordiazepoxide	0.76 g	0.71 g	0.65 g	0.52 g	0.47 g	
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate	0.12 g	0.12 g	0.11 g	0.09 g	0.09 g	
Cloxazolam						
Delorazepam						
Diazepam	22.15 mg	23.50 mg	23.22 mg	16.66 mg	19.34 mg	
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam	1.28 mg	6.62 mg	11.94 mg	14.66 mg	14.00 mg	
Flurazepam	2.29 g	2.15 g	2.04 g	1.70 g	1.54 g	
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam						
Loprazolam						
Lormetazepam						
Medazepam	0.17 g	0.14 g	0.13 g	0.10 g	0.08 g	
Nimetazepam						
Nitrazepam	18.72 mg	19.07 mg	18.52 mg	17.19 mg	17.09 mg	
Nordezepam						
Oxozolam						
Oxazepam	1.11 g	1.39 g	1.58 g	1.58 g	1.72 g	
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

TABLE 3(ii)
Consumption Figures from Various Countries (in Kg. unless stated)

Country	PAKISTAN					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam		25	25	2.868	2.868	
Camazepam						
Chlordiazepoxide						
Clobazam		30	30	20	20	40
Clonazepam						
Clotiazepam						
Clorazepane						
Cloxazolam						
Delorazepam						
Diazepam		435	435	2567	612	2783
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam						
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam		13	13	3	3	
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam						
Nitrazepam		7.15	7.15	3.75	3.75	
Nordezepam						
Oxozolam						
Oxazepam	15	15	45	45	20	
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	PHILLIPINES					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam	NM	NM	NM	NM	NM	
Camazepam						
Chlordiazepoxide	10.298	22.731	31.375			NA
Clobazam						
Clonazepam		0.091	0.566			NA
Clotiazepam						
Clorazepate	0.476	1.310	0.754			NA
Cloxazolam						
Delorazepam						
Diazepam		26.373	29.237	32.032	7743.4* 304(30c. c.bot.) 428045(10 mg) (2c.c amp)	
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam	NM	NM	NM	NM	NM	
Flurazepam	24.018	32.070	29.104	1531.7*	1720*	NA
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam	2.905	2.796	3.012	2029.2*		2139.5*
Loprazolam						
Lormetazepam						
Medazepam	2.177	2.351	0.966			NA
Nimetazepam						
Nitrazepam	4.055	0.925	1.102	1.85	3.14	NA
Nordezepam						
Oxozolam	NM	NM	NM	NM	NM	
Oxazepam	4.995	5.105	5.511	119.2*	266.8*	86.3*
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam	NM	NM	NM	NM		
Temazepam	NM	NM	NM	NM	NM	
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

* in thousands units (D.U)

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	SINGAPORE					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam		1.129		1.228	0.622	
Bromazepam						
Camazepam						
Chlordiazepoxide		2.308	1.952	2.290	1.026	
Clobazam						
Clonazepam		0.071	0.071	0.069	0.048	
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam		4.383	3.578	3.528	1.945	
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam		0.596	0.081	0.086	0.038	
Flurazepam		6.364	7.980	9.002	4.970	
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam						
Loprazolam						
Lormetazepam						
Medazepam		1.747	1.363	1.198	0.549	
Nimetazepam						
Nitrazepam		2.504	2.593	2.719	1.410	
Nordezepam						
Oxozolam	NM	NM	NM	NM	NM	
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 3 (ii)
Consumption Figure from Various Countries (in kg. unless stated)

Country	THAILAND					
Drug Type	**1977**	**1978**	**1979**	**1980**	**1981**	**1982**
Alprazolam						
Bromazepam	NM	NM	NM	NM	NM	
Camazepam						
Chlordiazepoxide				4.020		
Clobazam						
Clonazepam	NM	NM	NM	NM	NM	
Clotiazepam						
Clorazepate	NM	NM	NM	NM	NM	
Cloxazolam						
Delorazepam						
Diazepam				6.762		
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam	NM	NM	NM	NM	NM	
Flurazepam				1.328		
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam				0.162		
Loprazolam						
Lormetazepam						
Medazepam				0.943		
Nimetazepam						
Nitrazepam				1.118		
Nordezepam						
Oxozolam					0.175	
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam				0.385		
Temazepam				0.125		
Tofisopam						
Tetrazepam						
Triazolam						
Tibenzonium hydroxide						
Zopiclone						

Table 4(i)
Illicit Traffic (1979-1982)

Country / Drug Type	Argentina	Australia	Austria	Bahrain	Belgium	Brazil	Bulgaria	Burma	Canada	Central African Republic	Chile
Bromazepam	x	x									
Chlordiazepoxide		x									x
Clobazam	x										
Clonazepam											
Clorazepate											
Cloxazolam											
Diazepam		x	x			x		x	x		x
Estazolam											
Flunitrazepam	x	x									
Flurazepam		x									x
Lorazepam											
Medazepam		x									
Nimetazepam											
Nitrazepam		x									
Oxazepam		x									
Oxazolam											
Prazepam											
Temazepam											
Triazolam											

Table 4(i)
Illicit Traffic (1979-1982)

Country / Drug Type	Congo	Cuba	Cyprus	Czechos-lovakia	Denmark	Djibouti	Dominucia	Egypt	Equatorial Guinea	Fiji	Finland	France
Bromazepam								x				x
Chlordiazepoxide			x									
Clobazam								x				x
Clonazepam												
Clorazepate			x									
Cloxazolam												
Diazepam			x		x							
Estazolam												
Flunitrazepam											x	
Flurazepam					x							
Lorazepam												
Medazepam			x									
Nimetazepam												
Nitrazepam					x							
Oxazepam			x									
Oxazolam												
Prazepam												
Temazepam												
Triazolam												

Table 4(i)
Illicit Traffic (1979-1982)

Country / Drug Type	German Democratic Republic	Fed. Rep. of Germany	Greece	Guatemala	Haiti	Hong Kong	Honduras	Hungary	Iceland	India	Ireland
Bromazepam						x					
Chlordiazepoxide		x				x					
Clobazam		x				x					
Clonazepam						x					
Clorazepate											
Cloxazolam											
Diazepam		x	x	x		x					x
Estazolam											
Flunitrazepam				x		x					
Flurazepam						x					x
Lorazepam						x					x
Medazepam		x				x					
Nimetazepam				x		x					x
Nitrazepam											
Oxazepam						x					x
Oxazolam		x									
Prazepam						x					
Temazepam											
Triazolam						x					

Table 4(i)
Illicit Traffic (1979-1982)

Country / Drug Type	Iraq	Italy	Isreal	Japan	Kuwait	Lebanon	Leichtenstein	Luxembourg	Malaysia	Madagascar	Malta
Bromazepam			x	x							
Chlordiazepoxide					x				x		
Clobazam			x						x		
Clonazepam											
Clorazepate					x						
Cloxazolam				x							
Diazepam		x			x				x		x
Estazolam				x							
Flunitrazepam				x					x		x
Flurazepam									x		x
Lorazepam		x							x		
Medazepam									x		
Nimetazepam				x							
Nitrazepam									x		
Oxazepam									x		
Oxazolam											
Prazepam			x						x		
Temazepam											
Triazolam											

Table 4(i)
Illicit Traffic (1979-1982)

Country / Drug Type	Maldives	Monaco	New Zealand	Norway	Pakistan	Panama	Papua New Guinea	Peru	Philippines	Poland	Portugal
Bromazepam											
Chlordiazepoxide			x	x					x		x
Clobazam											
Clonazepam				x							x
Clorazepate			x						x		x
Cloxazolam											
Diazepam			x	x				x	x		x
Estazolam											
Flunitrazepam				x							x
Flurazepam				x					x		x
Lorazepam			x								x
Medazepam				x							x
Nimetazepam											
Nitrazepam			x	x					x	x	x
Oxazepam			x	x							x
Oxazolam											
Prazepam											
Temazepam											
Triazolam											

Table 4(i)
Illicit Traffic (1979-1982)

Country / Drug Type	Qatar	Republic of Korea	Senegal	Seychelles	Singapore	South Africa	Spain	Sri Langka	Sweden	Switzerland
Bromazepam										
Chlordiazepoxide						x		x	x	x
Clobazam										
Clonazepam									x	
Clorazepate										
Cloxazolam										
Diazepam						x	x	x	x	x
Estazolam										
Flunitrazepam					x		x		x	
Flurazepam						x				x
Lorazepam						x				x
Medazepam						x				x
Nimetazepam					x					
Nitrazepam						x			x	x
Oxazepam						x	x		x	
Oxazolam										
Prazepam						x				
Temazepam										
Triazolam					x					

Table 4(i)
Illicit Traffic (1979-1982)

Drug Type \ Country	Tonga	Trinidad & Tobago	Tunisia	Turkey	Tuvalu	U.S.S.R.	United Arab Emirates	United Kingdom
Bromazepam								
Chlordiazepoxide								
Clobazam							x	x
Clonazepam								x
Clorazepate								x
Cloxazolam								
Diazepam							x	x
Estazolam								
Flunitrazepam								x
Flurazepam								x
Ketazolam			x					
Lorazepam								x
Medazepam								
Nimetazepam								x
Nitrazepam							x	
Oxazepam								x
Oxazolam								x
Prazepam								
Temazepam								x
Triazolam								x

Table 4(i)
Illicit Traffic (1979-1982)

Drug Type \ Country	United Republic of Cameroon	U.S.A	Uruguay	Vanuatu	Yogoslavia	Zambia
Bromazepam						
Chlordiazepoxide		x				
Clobazam						
Clonazepam		x				
Clorazepate		x				
Cloxazolam						
Diazepam		x				
Estazolam						
Flunitrazepam		x	x			
Flurazepam		x				
Lorazepam		x				
Medazepam		x				
Nimetazepam						
Nitrazepam		x				
Oxazepam		x				
Oxazolam						
Prazepam		x				
Temazepam		x				
Triazolam						

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	AUSTRALIA			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide	18 cap, 191 tab			
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	14 amp 592 tab, 5.1 gm	31 amp 165 tab	263 tab 18.8 amp 5500 gm 451 D.U.	
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam			25 tab, 8 mg	
Flurazepam	36 cap			
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam	55 tab			
Nimetazepam			799 D.U.	
Nitrazepam	179 tab	40 tab	798 tab, 1 amp	
Nordezepam				
Oxozolam				
Oxazepam	362 tab	148 tab	764 tab	
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	AUSTRIA			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	165 tap 7 amp	4 amp		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	CANADA			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam				862 282,340 tab 109,474 kg 100 kg 6,200 D.U.
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	CYPRUS			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide	131 mg			
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	813 mg			
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam	Traces			
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam	Traces			
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	DEMOCRATIC REPUBLIC OF GERMANY			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide		15 cap 5 tab		
Clobazam			50 tab	
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	20 mg, 9 amp 567 tab	648 tab		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam		100 tab		
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	DENMARK			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	841 tab	347 tab	162 D.U.	347 D.U.
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				13 D.U.
Nitrazepam	16 tab	13 tab		
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	FEDERAL REPUBLIC OF GERMANY			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide		20		
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam		648		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam		1000		
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	FINLAND			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				1 D.U.*
Clotiazepam				
Clorazepate			2 D.U.*	121 D.U.*
Cloxazolam				
Delorazepam				
Diazepam			235 D.U.*	2627 D.U.*
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam			116 D.U.	
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam			326 D.U.	260 D.U..
Loprazolam				
Lormetazepam				
Medazepam			127 D.U.	
Nimetazepam				
Nitrazepam			9 D.U.	114 D.U.
Nordezepam				
Oxozolam				
Oxazepam			75 D.U.	6546 D.U.
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

*D.U. – Dosage Units.

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	HONG KONG			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam		22 tab	99 tab	76 D.U.
Camazepam				
Chlordiazepoxide	8903 tab	4472 tab		16519 D.U.
Clobazam		28 tab	161 tab	92 D.U.
Clonazepam	30 tab	21 tab		
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	1186 tab	83266 tab 9.5 g powder	18220 D.U.	5808 D.U.
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam		5 tab	130 tab	128 D.U.
Flurazepam	503 tab	57 tab		68 D.U.
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam	276 tab	792 D.U.	193 D.U.	
Loprazolam				
Lormetazepam				
Medazepam	300 tab			10 D.U.
Nimetazepam				
Nitrazepam	1336 tab	392 tab	1685 D.U.	3198 D.U.
Nordezepam				
Oxozolam			167 D.U.	16 D.U.
Oxazepam	646 tab	60 tab		324 D.U.
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam	300 tab			
Temazepam		9 tab	18 D.U.	5 D.U.
Tofisopam				
Tetrazepam				
Triazolam		3 tab	13 tab	37 D.U.
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	IRELAND			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam		954 tab		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam		1129 tab		
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam	1 tab			
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam	2 tab			
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam	1 tab			
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	JAPAN			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam		15 g		
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam			292	
Delorazepam				
Diazepam				
Estazolam		12 g		
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam		7 g		
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	KUWAIT			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				10 D.U.
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam				
Estazolam				384 D.U.
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				2 D.U.
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	LUXEMBOURG			
Drug Tpye	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam			2000 D.U.	
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				7 D.U.
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	MALAYSIA			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam			1143 D.U.	24 D.U.
Camazepam				
Chlordiazepoxide	17712 tab	12388 tab	19362 D.U.	6521 D.U.
Clobazam			950 D.U.	138 D.U.
Clonazepam	2 tab	2 tab	1235 D.U.	
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	9445 tab	13620 tab	20693 D.U.	9418 D.U.
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam			15821 D.U.	464 D.U.
Flurazepam	10 tab	37 tab	589 D.U.	
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam	948 tab	86 tab	2633 D.U.	1085 D.U.
Loprazolam				
Lormetazepam				
Medazepam	160 tab		75 D.U.	
Nimetazepam			265 D.U.	
Nitrazepam	585 tab	313 tab	1280 D.U.	751 D.U.
Nordezepam				
Oxozolam				
Oxazepam	56 tab			12 D.U.
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam	133 tab			240 D.U.
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam			985 D.U.	32152 D.U.
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	MALTA			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	200 tab			
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam		2 tab		
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, & 1982

Country	MEXICO			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam			10kg bulk	
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Coutry	NORWAY			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam				
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam		15 tab	148 tab	
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	NEW ZEALAND			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide	31 D.U.	46 D.U.		
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate	1			
Cloxazolam				
Delorazepam				
Diazepam	714 D.U.	2621 D.U.		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam	112 D.U.	60 D.U.		
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam	245 D.U.	261 D.U.		
Nordezepam				
Oxozolam				
Oxazepam	71 D.U.	146 D.U.		
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	PHILIPPINES			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	239, 256 D.U.	2326 D.U.	973 D.U.	20960 D.U.
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam	338 D.U.	46 D.U.		
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				164 D.U.
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam			54070 D.U.	100337 D.U.
Nitrazepam	65432 D.U.	6766 D.U.		
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	PORTUGAL			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide	650 cap			
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate	663 tab 10 cap, 5 amp	31 cap		
Cloxazolam				
Delorazepam				
Diazepam				
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam		340 tab	1767tab	
Flurazepam	150cap	257 cap		
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam	96 tab	398 tab		
Loprazolam				
Lormetazepam				
Medazepam	25cap	189 cap		
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam	45 tab	10 tab		
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Coutry	SINGAPORE			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam			2 D.U.	
Camazepam				
Chlordiazepoxide			4 D.U.	
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam			729 D.U.	553 D.U.
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam		15006 tab	36001 tab	7078 tab
Flurazepam			7 D.U.	38 D.U.
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam		6 D.U.		
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam		2 D.U.		68 D.U.
Nitrazepam		60 D.U.		70 D.U.
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam		60 D.U.		243 D.U.
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Coutry	SOUTH AFRICA			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide		106		
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam		34682		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam		10		
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam		197		
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1979, 1980, 1981 & 1982

Country	SRI LANKA			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide			333 D.U.	
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	190 tab	66 tab		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(ii)(a)
Illicit Traffic
Amount of Seizures for 1974, 1975, 1976 & 1983

Country	UNITED STATES OF AMERICA		
Drug Type	**Jan 1, 1974 to May 24, 1983**	**July 2, 1975 to May 24, 1983**	**Dec 13, 1976 to May 24, 1983**
Alprazolam			
Bromazepam			
Camazepam			
Chlordiazepoxide		1,54,322 D.U.	
Clobazam			
Clonazepam		163 D.U.	
Clotiazepam			
Clorazepate		963 D.U.	
Cloxazolam			
Delorazepam			
Diazepam		8.7 million D.U.	
Estazolam			
Etifoxine			
Ethyl loflazepate			
Fludiazepam			
Flunitrazepam	205 D.U.		
Flurazepam		21,713 D.U.	
Halazepam	2 D.U.		
Haloxozolam			
Ketazolam			
Lorazepam		10,226 D.U.	
Loprazolam			
Lormetazepam			
Medazepam	9,313 D.U.		
Nimetazepam			
Nitrazepam	109,626 D.U.		
Nordezepam	20 D.U.		
Oxozolam			
Oxazepam		2,059 D.U.	
Pinazepam			
Pirenzepam			
Propizepine			
Prazepam			19,036 D.U.
Temazepam	5 D.U.		
Tofisopam			
Tetrazepam			
Triazolam			
Tibenzonium hydroxide			
Zopiclone			

Table 4(ii)(b) Number of Seizures

Country	Australia		Canada		Hong Kong	
Drug Type	**1981**	**1982**	**1981**	**1982**	**1981**	**1982**
Alprazolam						
Bromazepam					3	2
Camazepam					50	17
Chlordiazepoxide					2	1
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam	24		319	282	84	32
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam					7	6
Flurazepam						2
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam					7	4
Loprazolam						
Lormetazepam						
Medazepam						1
Nimetazepam	17					
Nitrazepam					8	22
Nordezepam						
Oxozolam					1	1
Oxazepam	35					1
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam					1	1
Tofisopam						
Tetrazepam						
Triazolam					3	4
Tibenzonium hydroxide						
Zopiclone						

Table 4(ii)(b) Number of Seizures

Country	Kuwait		Luxembourg		Malaysia	
Drug Type	**1981**	**1982**	**1981**	**1982**	**1981**	**1982**
Alprazolam						
Bromazepam					4	1
Camazepam					28	11
Chlordiazepoxide					1	2
Clobazam		1			3	
Clonazepam						
Clotiazepam						
Clorazepate						
Cloxazolam						
Delorazepam						
Diazepam		25			21	47
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam		1		1	36	65
Flurazepam					3	
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam	1				3	7
Loprazolam						
Lormetazepam						
Medazepam					1	
Nimetazepam						
Nitrazepam	3				7	8
Nordezepam						
Oxozolam						
Oxazepam						1
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						1
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam					3	28
Tibenzonium hydroxide						
Zopiclone						

Table 4(ii)(b) Number of Seizures

Country	Philippines		Saudi Arabia		Singapore	
Drug Type	**1981**	**1982**	**1981**	**1982**	**1981**	**1982**
Alprazolam						
Bromazepam					1	
Camazepam						
Chlordiazepoxide						
Clobazam						
Clonazepam						
Clotiazepam						
Clorazepate				3		
Cloxazolam						
Delorazepam						
Diazepam	9	18		3	47	46
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam					260	
Flurazepam					1	4
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam	1				1	
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam	25	28			1	11
Nitrazepam						9
Nordezepam						
Oxozolam						
Oxazepam						
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam					9	26
Tibenzonium hydroxide						
Zopiclone						

Table 4(ii)(b) Number of Seizures

Country	Sri Lanka		Sweden		Thailand	
Drug Type	**1981**	**1982**	**1981**	**1982**	**1981**	**1982**
Alprazolam						
Bromazepam		4			36	32
Camazepam						
Chlordiazepoxide			6	6		
Clobazam						
Clonazepam				1		
Clotiazepam						
Clorazepate			14	20		
Cloxazolam						
Delorazepam						
Diazepam			162	199		34
Estazolam						
Etifoxine						
Ethyl loflazepate						
Fludiazepam						
Flunitrazepam			4	8		
Flurazepam						
Halazepam						
Haloxozolam						
Ketazolam						
Lorazepam		7				
Loprazolam						
Lormetazepam						
Medazepam						
Nimetazepam						
Nitrazepam	88	124	20	11		
Nordezepam						
Oxozolam						
Oxazepam	53	50				
Pinazepam						
Pirenzepam						
Propizepine						
Prazepam						
Temazepam						
Tofisopam						
Tetrazepam						
Triazolam						1
Tibenzonium hydroxide						
Zopiclone						

Table 4(ii)(b) Number of Seizures

Country	United Kingdom	
Drug Type	**1981**	**1982**
Alprazolam		
Bromazepam		1
Camazepam		
Chlordiazepoxide	42	40
Clobazam	22	
Clonazepam	1	
Clotiazepam		
Clorazepate	9	9
Cloxazolam		
Delorazepam		
Diazepam	276	237
Estazolam		
Etifoxine		
Ethyl loflazepate		
Fludiazepam		
Flunitrazepam	13	3
Flurazepam	47	50
Halazepam		
Haloxozolam		
Ketazolam	2	7
Lorazepam	27	43
Loprazolam		
Lormetazepam	1	3
Medazepam	3	1
Nimetazepam		
Nitrazepam	104	83
Nordezepam		
Oxozolam		
Oxazepam	6	2
Pinazepam		
Pirenzepam		
Propizepine		
Prazepam		
Temazepam	23	26
Tofisopam		
Tetrazepam		
Triazolam	22	11
Tibenzonium hydroxide		
Zopiclone		

Table 4(iii)

Country	Are Benzodiazepines Available in Your Market	Does A Benzodiazepine Abuse Problem Edangering Public Health Exist	Has Illicit Traffic Been Reported
Australia	x	x	x
Austria	x		x
Bahrain	x		N/I
Belgium	x	x	N/I
Brazil	x		N/I
Bulgaria	x		
Burma	x	x	
Canada	x		x
Central African Republic	x	N/I	N/I
Chile	x		
Congo	x	N/I	N/I
Cuba	x		N/I
Cyprus	x	x	N/I
Czechoslovakia	x	N/I	
Denmark	x	x	N/I
Djibouti	x	N/I	N/I
Dominica	x		
Egypt	x	x	N/I
Equatorial Guinea	x	N/I	N/I
Fiji	x	N/I	
France	x	x	N/I
German Democratic Republic	x		N/I
Federal Republic of Germany	x		x
Greece	x		x
Guatemala	x	N/I	x
Haiti	x		
Honduras	x		N/I
Hong Kong	x	x	x
Hungary	x		N/I
Iceland	x	N/I	N/I
Iraq	x	N/I	
Ireland	x	N/I	N/I
India	x		
Indonesia	x	x	N/I
Japan	x		N/I
Kuwait	x	N/I	

(connt...)

Table 4(iii)

Country	Are Benzodiazepines Available in Your Market	Does A Benzodiazepine Abuse Problem Edangering Public Health Exist	Has Illicit Traffic Been Reported
Lebanon	x	N/I	
Luxembourg	x	N/I	
Leichtenstein	x	N/I	
Madagascar	x	x	
Maldives	x	N/I	
Malaysia	x		x
Monaco	x	N/I	N/I
New Zealand	x		
Norway	x	N/I	N/I
Pakistan	x		N/I
Panama	x		
Papua New Guinea	x		
Peru	x	N/I	x
Philippines	x	x	x
Poland	x		
Qatar	x	N/I	
Republic of Korea	x		N/I
Senegal	x		N/I
Seychelles	x		
Singapore	x	N/I	
South Africa	x	N/I	
Spain	x	x	x
Sri Lanka	x	N/I	x
Sweden	x	x	x
Switzerland	x		N/I
Thailand	x	x	
Tonga	x		
Trinidad & Tobago	x		
Turkey	x	x	N/I
Tunisia	x		
Tuvalu	x		
United Arab Emirates	x	N/I	N/I
U.S.S.R.	x		
United Kingdom	x	N/I	x
United Republic of Cameroon	x	N/I	N/I
U.S.A.	x	x	x
Vanuatu	x	N/I	
Yugoslavia	x	N/I	
Zambia	x		

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Drug Type / Country	Alprazolam	Bromazepam	Camazepam	Chlordiazepoxide	Clobazam	Clonazepam	Clorazepate
Australia		x					
Austria		x					
Bahrain							
Belgium							
Brazil							
Burma							
Canada							
Central African Republic							
Chile							
Cuba							
Cyprus							
Denmark	x	x					
Egypt		x			x		
France		x		x	x		
German Democratic Republic							
Germany Federal Republic of							
Greece							
Guatamala							
Honduras					x		
Hungary							
India							
Iran				x			
Iraq							
Japan							
Kuwait							
Madagascar					x		
Malaysia							
Maldives							
New Zealand							
Norway							

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Drug Type / Country	Alprazolam	Bromazepam	Camazepam	Chlordiazepoxide	Clobazam	Clonazepam	Clorazepate
Pakistan							
Papua New Guinea							
Peru							
Philippines		x					
Poland						x	
Portugal							
Qatar		x					
Republic of Korea							
Senegal							
Singapore							
South Africa							
Sri Lanka							
Spain				x			
Sweden							
Switzerland	x						
Trinidad & Tobago					x		
Turkey							
Tuvalu				x		x	
USSR							
United Arab Emirates							
United Kingdom							
United States of America							
Vanuatu				x		x	x
Yogoslavia							
Zambia							
Total No. of Abuse By Country	2	7	0	5	5	3	1

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Drug Type / Country	Clotiazepam	Cloxazolam	Diazepam	Estazolam	Fludiazepam	Flunitrazepam	Flurazepam	Halazepam
Australia			x			x		
Austria			x			x		
Bahrain			x			x		
Belgium								
Brazil								
Burma			x					
Canada			x					
Central African Republic								
Chile								
Cuba								
Cyprus			x					
Denmark		x		x		x		
Egypt								
France								
German Democratic Republic								
Germany Federal Republic of								
Greece								
Guatamala						x		
Honduras						x		
Hungary								
India								
Iran			x				x	
Iraq								
Japan								
Kuwait								
Madagascar								
Malaysia						x		
Maldives								
New Zealand								
Norway								

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Country / Drug Type	Clotiazepam	Cloxazolam	Diazepam	Estazolam	Fludiazepam	Flunitrazepam	Flurazepam	Halazepam
Pakistan								
Papua New Guinea								
Peru								
Philippines			x				x	
Poland								
Portugal								
Qatar						x		
Republic of Korea								
Senegal								
Singapore						x		
South Africa								
Sri Lanka			x					
Spain			x					
Sweden			x					
Switzerland								
Trinidad & Tobago								
Turkey						x	x	
Tuvalu			x					
USSR								
United Arab Emirates								
United Kingdom								
United States of America			x				x	
Vanuatu								
Yogoslavia								
Zambia								
Total No. of Abuse By Country	0	1	13	1	0	11	4	0

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Drug Type / Country	Ketazolam	Loprazolam	Lorazepam	Lormetazepam	Medazepam	Nimetazepam	Nitrazepam	Nordazepam
Australia			x				x	
Austria							x	
Bahrain			x				x	
Belgium								
Brazil								
Burma								
Canada								
Central African Republic								
Chile								
Cuba								
Cyprus								
Denmark								
Egypt								
France								
German Democratic Republic								
Germany Federal Republic of								
Greece								
Guatamala								
Honduras								
Hungary								
India								
Iran			x				x	
Iraq								
Japan								
Kuwait								
Madagascar								
Malaysia								
Maldives								
New Zealand								
Norway								

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Drug Type / Country	Ketazolam	Loprazolam	Lorazepam	Lormetazepam	Medazepam	Nimetazepam	Nitrazepam	Nordazepam
Pakistan				x				
Papua New Guinea								
Peru								
Philippines			x				x	
Poland								
Portugal								
Qatar								
Republic of Korea								
Senegal								
Singapore								
South Africa								
Sri Lanka								
Spain								
Sweden			x				x	
Switzerland	x							
Trinidad & Tobago								
Turkey			x		x		x	
Tuvalu								
USSR								
United Arab Emirates								
United Kingdom								
United States of America			x				x	
Vanuatu								
Yogoslavia								
Zambia								
Total No. of Abuse By Country	1	0	7	1	1	0	9	0

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Drug Type / Country	Oxazepam	Oxazolam	Pinazepam	Pirenzepam	Prazepam	Temazepam	Tetrazepam	Tofizopam	Triazolam
Australia		x							
Austria		x							
Bahrain									
Belgium									
Brazil									
Burma									
Canada									
Central African Republic									
Chile									
Cuba									
Cyprus									
Denmark									x
Egypt									
France									
German Democratic Republic									
Germany Federal Republic of									
Greece									
Guatamala									
Honduras									
Hungary									
India									
Iran	x								
Iraq									
Japan									
Kuwait									
Madagascar									
Malaysia									
Maldives									
New Zealand									
Norway									

Table 4(iv)
ABUSE OF DRUGS BY COUNTRY

Drug Type / Country	Oxazepam	Oxazolam	Pinazepam	Pirenzepam	Prazepam	Temazepam	Tetrazepam	Tofizopam	Triazolam
Pakistan									
Papua New Guinea									
Peru									
Philippines	x	x						x	
Poland									
Portugal									
Qatar									
Republic of Korea									
Senegal									
Singapore									
South Africa									
Sri Lanka									
Spain									
Sweden	x								
Switzerland									
Trinidad & Tobago									
Turkey	x	x			x	x			
Tuvalu									
USSR									
United Arab Emirates									
United Kingdom									
United States of America	x				x	x			
Vanuatu									
Yogoslavia									
Zambia									
Total No. of Abuse By Country	5	4	0	0	2	2	0	0	2

TABLE 4(v)
Abuse Data Number of Cases

	No. of Cases of Abuse	AUSTRALIA			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	112			
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam	50			
Nordezepam				
Oxozolam				
Oxazepam	138			
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

TABLE 4(v)
Abuse Data Number of Cases

No. of Cases of Abuse	CHILE			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide		1		
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam		1		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

TABLE 4(v)
Abuse Data Number of Cases

No. of Cases of Abuse	CYPRUS			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide		5		
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate		1		
Cloxazolam				
Delorazepam				
Diazepam		13		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam	1			
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam	1			
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

TABLE 4(v)
Abuse Data Number of Cases

Drug Type	No. of Cases of Abuse HONG KONG 1979	1980	1981	1982
Alprazolam				
Bromazepam			3	2
Camazepam				
Chlordiazepoxide	20	21	50	17
Clobazam			2	1
Clonazepam	1	1		
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam	40	40	84	32
Estazolam				
Etifoxine				
Fludiazepam				
Flunitrazepam			7	6
Flurazepam				2
Halazepam				
Ketazolam				
Lorazepam	7	4		
Loprazolam				
Lormetazepam				1
Medazepam				
Nimetazepam				
Nitrazepam	8	22		
Nordezepam				
Oxozolam	1	1		
Oxazepam				1
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam	1	1		
Tofisopam				
Tetrazepam				
Triazolam	3	4		
Tibenzonium hydroxide				
Zopiclone				

TABLE 4(v)
Abuse Data Number of Cases

Drug Type	No. of Cases of Abuse KUWAIT 1979	1980	1981	1982
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide	1	7		
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate		1		
Cloxazolam				
Delorazepam				
Diazepam	14	15		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

TABLE 4(v)
Abuse Data Number of Cases

No. of Cases of Abuse / Drug Type	PHILIPPINES 1979	1980	1981	1982
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam			35	31
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam			375	532
Diazepam				
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam			145	158
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam			71	79
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam			140	166
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				118
Zopiclone				

TABLE 4(v)
Abuse Data Number of Cases

No. of Cases of Abuse / Drug Type	SINGAPORE 1979	1980	1981	1982
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide				
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam				
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam			175	
Flurazepam				
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam				
Nordezepam				
Oxozolam				
Oxazepam				
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

TABLE 4(v)
Abuse Data Number of Cases

No. of Cases of Abuse	SWITZERLAND			
Drug Type	**1979**	**1980**	**1981**	**1982**
Alprazolam				
Bromazepam				
Camazepam				
Chlordiazepoxide		1		
Clobazam				
Clonazepam				
Clotiazepam				
Clorazepate				
Cloxazolam				
Delorazepam				
Diazepam		2		
Estazolam				
Etifoxine				
Ethyl loflazepate				
Fludiazepam				
Flunitrazepam				
Flurazepam	4	1		
Halazepam				
Haloxozolam				
Ketazolam				
Lorazepam				
Loprazolam				
Lormetazepam				
Medazepam				
Nimetazepam				
Nitrazepam		1		
Nordezepam				
Oxozolam				
Oxazepam	3	1		
Pinazepam				
Pirenzepam				
Propizepine				
Prazepam				
Temazepam				
Tofisopam				
Tetrazepam				
Triazolam				
Tibenzonium hydroxide				
Zopiclone				

Table 4(v)
Abuse Data Number of Cases

No. of Cases of Abuse	UNITED STATES OF AMERICA		
Drug Type	**Jan 1, 1974 to May 24, 1983**	**July 2, 1975 to May 24, 1983**	**Dec 17, 1976 to May 24, 1983**
Alprazolam			
Bromazepam			
Camazepam			
Chlordiazepoxide		234	
Clobazam			
Clonazepam		3	
Clotiazepam			
Clorazepate		40	
Cloxazolam			
Delorazepam			
Diazepam		1,815	
Estazolam			
Etifoxine			
Ethyl loflazepate			
Fludiazepam			
Flunitrazepam	3		
Flurazepam		125	
Halazepam	1		
Haloxozolam			
Ketazolam			
Lorazepam		19	
Loprazolam			
Lormetazepam			
Medazepam	3		
Nimetazepam			
Litrazepam	23		
Nordezepam	1		
Oxozolam			
Oxazepam		39	
Pinazepam			
Pirenzepam			
Propizepine			
Prazepam			13
Temazepam	2		
Tofisopam			
Tetrazepam			
Triazolam			
Tibenzonium hydroxide			
Zopiclone			

Table 4(vi)
Table Showing General Drug Abuse, Opiate Abuse, Benzodiazepine Abuse and Pentazocine Abuse in 1980, 1981 & 1982

Country	Population (in million)	No. of Persons Arrested for General Drug Abuse		No. of Persons Arrested for Opiate Abuse		No. of Cases of Benzodiazepines Abuse		No. of Cases of Pentazocine Abuse	
		1980	1981	1980	1981	1980	1981	1981	1982
Algeria	18.59	461	539			N/I			
Argentina	27.06	2,023	2,790	60	1,174	N/I			
Australia	14.62	23,764	19,484	2,032	2,170	300			
Austria	7.56	4,900	2,102	1,422					
Bangladesh	87.66	290	296	33	26				
Barbados	0.25	226	261						
Belgium	9.86	1,630	189	45	36				
Brazil	123.03	2,498	3,040			N/I			
Bulgaria	8.86	N/I	25	N/I	41				
Burma	35.3	2,748	2,918	2,345	2,492				
Burundi	4.51	N/I		N/I					
Cameroon		84	106						

Table 4(vi)
Table Showing General Drug Abuse, Opiate Abuse, Benzodiazepine Abuse and Pentazocine Abuse in 1980, 1981 & 1982

Country	Population (in million)	No. of Persons Arrested for General Drug Abuse		No. of Persons Arrested for Opiate Abuse		No. of Cases of Benzodiasepine Abuse		No. of Cases of Pentazocine Abuse	
		1980	1981	1980	1981	1980	1981	1981	1982
Canada	23.94	38,498	56,224	436	1,010		200		
Chile	11.10	1,889	1,740		58	2			
Colombia	27.09	1,492	892			N/I			
Costa Rica	2.24		107			N/I			
Cyprus	0.63	43	46	2		21			
Czechoslovakia	15.32	6	55						
Denmark	5.12	3,126		N/I					
Djibouti	N/I	3	26	N/I					
Egypt	41.99	8,658	7,107	N/I					
Finland	4.78	N/I	364	N/I					
France	53.71	10,958	13,850	3,610	5,330	N/I			

Table 4(vi)
Table Showing General Drug Abuse, Opiate Abuse, Benzodiazepine Abuse and Pentazocine Abuse in 1980, 1981 & 1982

Country	Population (in million)	No. of Persons Arrested for General Drug Abuse		No. of Persons Arrested for Opiate Abuse		No. of Cases of Benzodiazepines Abuse		No. of Cases of Pentazocine Abuse	
		1980	1981	1980	1981	1980	1981	1981	1982
French Polynesia	0.16	126	165						
German Democratic Republic	16.74	63	38	25	17				
German Federal Republic	61.56	55,447	56,388	N/I	18,100			228	259
Greece	9.6	536	732	54	224				
Grenada	0.10	112							
Guyana	0.10	112	120						
Honduras	3.69	264	463						
Hong Kong	5.07		7,649		7,553	62	166	7	22
Hungary	10.71	N/I	4	N/I	2				

Table 4(vi)
Table Showing General Drug Abuse, Opiate Abuse, Benzodiazepine Abuse and Pentazocine Abuse in 1980, 1981 & 1982

Country	Population (in million)	No. of Persons Arrested for General Drug Abuse		No. of Persons Arrested for Opiate Abuse		No. of Cases of Benzodiazepines Abuse		No. of Cases of Pentazocine Abuse	
		1980	1981	1980	1981	1980	1981	1981	1982
Iceland	0.23	451		N/I					
India	66.36	1,058	1,205	737	770				
Indonesia	151.89	523	525	63	47	N/I			
Iran	37.45	2,623	4,342	N/I					
Iraq	12.08	4	13	N/I					
Italy	57.04	7,783	9,469	3,526	4,471				
Ivory Coast	7.97	N/I		N/I					
Jamaica	2.19	465	960						
Japan	116.78	21,793	23,720	56	48			204	
Jordan	3.19	21							
Kenya	16.4	6,448		N/I		N/I			
Korea	17.91	655	725	35	31	N/I			

Table 4(vi)
Table Showing General Drug Abuse, Opiate Abuse, Benzodiazepine Abuse and Pentazocine Abuse in 1980, 1981 & 1982

Country	Population (in million)	No. of Persons Arrested for General Drug Abuse		No. of Persons Arrested for Opiate Abuse		No. of Cases of Benzodiazepines Abus		No. of Cases of Pentazocine Abus	
		1980	1981	1980	1981	1980	1981	1981	1982
Kuwait	1.37	189	223	37	57	23			
Lebanon	3.16	263	251	115	109				
Lesotho	1.34	339	462	N/I					
Liechtenstein	0.03	28		5	11				
Luxemburg	0.36	66	387	47					
Madagascar	8.74	614	561						
Malaysia	13.44	5,660		4,962	7,444	1,070	360		
Malta	0.36	73			5				
Mauritius	0.69	356	426	91	132				
Mexico	71.91	2,883	4,063	443	387				
Monaco	0.03	35		9					

Table 4(vi)
Table Showing General Drug Abuse, Opiate Abuse, Benzodiazepine Abuse and Pentazocine Abuse in 1980, 1981 & 1982

Country	Population (in million)	No. of Persons Arrested for General Drug Abuse		No. of Persons Arrested for Opiate Abuse		No. of Cases of Benzodiazepines Abuse		No. of Cases of Pentazocine Abuse	
		1980	1981	1980	1981	1980	1981	1981	1982
Morocco	20.24	3,996	7,789	N/I	1				
Netherlands	14.14	7,153	8,409	2,917	3,764				
Netherlands Antilles	0.27	481	804	N/I	23				
New Caledonia	0.15	19		1					
New Zealand	3.10	6,257	8,017	N/I					
Nigeria	77.08	1,259	1,352	N/I					
Norway	4.09	4,048	4,757	N/I					
Pakistan	82.44	13,991	17,192	2,048	4,351				
Panama	1.84		1,251						
Philippines	48.40		3,100		2	N/I	766		
Poland	35.58	169	437	N/I	15				

Table 4(vi)
Table Showing General Drug Abuse, Opiate Abuse, Benzodiazepine Abuse and Pentazocine Abuse in 1980, 1981 & 1982

Country	Population (in million)	No. of Persons Arrested for General Drug Abuse		No. of Persons Arrested for Opiate Abuse		No. of Cases of Benzodiasepine Abuse		No. of Cases of Pentazocine Abuse	
		1980	1981	1980	1981	1980	1981	1981	1982
Tunisia	6.37	156	59						
Turkey	44.92	3,418	3,920	297	556				
Turks & Caicos Island		63	26			N/I		22	
United Kingdom	05.95	18,366	19,497	1,519	1,476			2	
U.S.A.	227,66	12,158	12,876	2,080	2,521				
U.S.S.R.	265.54	27	25	2	2				
Venezuela	13.91	993	576	2					
Yemen	5.93	N/I		N/I					
Yugoslavia	22.34	178	139	87	89				
Zambia	23.94	9							

LIST OF ORGANIZATIONS AND INDIVIDUAL CONTRIBUTORS.

1. Director General
   Department of Health
   P.O. Box 100
   Woden, A.C.T.
   Australia 2606

2. Ministry of Health
   Rangoon,
   Burma.

3. J.G. Le Cavalier
   Director
   Department of National Health and Welfare
   Bureau of Dangerous Drugs
   Health Protection Branch
   Ottawa
   Canada K1A 1B9.

4. Narcotics Division
   Security Branch
   Government Secretariat
   United Centre, 31st. Floor
   95, Queensway
   Hong Kong

5. Dr. S.S. Gothoskar
   Drugs Controller
   Directorate General of Health Services
   Nirman Bhavan
   Maulana Azad Road
   New Delhi
   India

6. Datuk (Dr.) Abdul Khalid bin Sahan
   Pemangku Ketua Pengarah Kesihatan
   Ministry of Health
   M.M.A. Building, Jalan Pahang
   Kuala Lumpur 02-14.

7. Director General
   Department of Health
   P.O. Box 5013
   Wellington
   New Zealand.

8. Director of Pharmaceutical Services
   Narcotics and Drug Abuse Control Unit
   Federal Ministry of Health
   P.M.P. 2007, Yaba
   Lagos, Nigeria.

9. Director of Public Health
   Pharmaceutical Division
   P.O. Box 8128 DEP
   Oslo 1
   Norway.

10. Mr. Pervez Rahman
    Deputy Director (Law)
    Pakistan Narcotic Control Board
    Islamabad
    Pakistan.

11. Manuel M. Supnet
Executive Director
Tuazon - Gonzales Building
356, Solana Street,
Intramuros
Manila
Philippines.

12. Director de la Pharmacie
Ministere de la Sante Publique
153, Rue Blanchot
Dakar
Senegal.

13. Director of Medical Services
Ministry of Health
55, Cuppage Centre #09-00
Singapore 0922.

14. Panya Vanasatiti
Director
Narcotic Control Division
Food and Drug Administration
Ministry of Public Health
Bangkok 2
Thailand.

15. Dr. V. Navaratnam
Associate Professor and Director
National Drug Research Centre
University of Science Malaysia
Penang
Malaysia.

16. Tan Siew Choon
Researcher/Pharmacist
National Drug Research Centre
University of Science Malaysia
Penang
Malaysia

17. Jeanette Jaya Chooi Gaik
Research Officer
National Drug Research Centre
University of Science Malaysia
Penang
Malaysia.